DISEASES *of the* CHEST

VOLUME XV MAY, 1949 NUMBER 5

Undergraduate and Postgraduate Teaching in Diseases of the Chest

A Report of the Joint Program of the New York Medical College and the Municipal Tuberculosis Sanatorium of the City of New York*

JAMES S. EDLIN, M.D., F.C.C.P.,** SYDNEY BASSIN, M.D., F.C.C.P.† and SAMUEL A. THOMPSON, M.D., F.C.C.P.††

New York, New York

Tuberculosis is an endemic disease that constantly presents the threat of increasing to epidemic proportions. The aftermath of war has amply demonstrated how that threat can become an actuality. The tremendous optimism that tuberculosis had at last reached a stage where control could be logically and rationally envisioned faded rapidly before the realities of destruction, displacement and deprivation. Again available forces have been marshalled to control the disease. Mass x-ray surveys, national and international Public Health Commissions, antibiotics—all are part of the armamentarium. The vast program can succeed only if adequately trained and sufficient personnel is available to administer it. The disease must be recognized early and facilities be made available for treatment. The bulwark of this program must be the physician upon whose training and skill the plan must stand or fall. It is not sufficient to have a trained body of specialists in tuberculosis. It would be almost impossible to obtain a sufficiently large number of such men. They must be the nucleus but they cannot possibly hope to cope with so gigantic a problem without the complete cooperation of the entire medical profession.

The general practitioner and the medical student who will be

*New York Medical College, Flower and Fifth Avenue Hospitals.
**Medical Director, Municipal Tuberculosis Sanatorium.
†Associate Attending Physician, Municipal Tuberculosis Sanatorium.
††Surgical Director, Municipal Tuberculosis Sanatorium.

Copyright, 1949, by the American College of Chest Physicians

the general practitioner or specialist of the future must be enlisted. Their importance has not gone unnoticed by those intensely interested in the struggle against tuberculosis. Tuberculosis Associations, chest specialists and the College Council have gone on record advocating more intensive and extensive instruction in tuberculosis. Barrier after barrier has been met. During the war years the speeded-up and concentrated medical school curriculum left no space for enlargement. This was a convincing argument but, unfortunately, the years since the war ended have brought only a slight improvement in the situation.

Although the great increase in detailed knowledge of the various parts of the body and their respective diseases has necessitated specialization no one knows better than the specialist that the general practitioner is the foundation rock of our profession. It is he who first sees the tuberculous patient when he is only slightly ill or even asymptomatic. His awareness of the possibility of the presence of tuberculosis in his patients can only result in earlier diagnosis and earlier and more effective therapy. The general practitioner, however, is not alone in his failure to keep the disease in mind. Specialists in other fields are just as prone to overlook its presence. How many times have we seen surgical and obstetrical cases with slight coughs who are operated upon or delivered without any but the most cursory and superficial attention paid to that symptom? How many times have we seen the diagnosis made only after the patient fails to make an uneventful recovery and presents a clinical picture of low grade fever, cough and expectoration?

Re-education must be made complete in all parts of our profession. There is certainly no intention to create a vast body of experts in pulmonary tuberculosis but, rather to create an awareness of the problem, an alertness to its possible presence, and a realization of the effectiveness of early therapy. We should like to see such an educational program instituted in every medical school and we look forward to the day when every hospital with a staff of well trained chest men can extend such teaching to all the men on the staff and in the community regardless of their specialty.

With this thought in mind we approached Dean J. A. W. Hetrick of the New York Medical College. The idea of an intensive course in tuberculosis for both medical students and postgraduate students was broached and discussed. The wholehearted reception accorded this suggestion was most encouraging and out of these meetings resulted an affiliation between the New York Medical College and the Municipal Sanatorium of the City of New York at Otisville, New York. For a beginning, the course was made an elective one

of three weeks duration for senior students during the summer months. The students were to be housed in the Staff House at the Sanatorium and teaching was to be done by the Medical Staff.

Ideally, the student should have an opportunity to observe the course of the disease over a long period of time so that its varied manifestations, its progression and healing, its treatment and emergencies might be thoroughly understood. Such a state of affairs is almost utopian in the already crowded medical school curriculum. It was our thought that an intensive course given in the atmosphere of the Sanatorium would arouse interest and dispel the unwarranted fear of the disease that exists among medical students and their practicing colleagues. By daily contact under skillful guidance a more rational approach to the disease would be instilled. The technique of isolation and the simple rules of personal protection would overcome the tuberculosis phobias so commonly encountered.

Although the course was made an elective one it was hoped that the students who took it would act as medical missionaries and would arouse enthusiasm in their fellow students. This very thing happened and the wonderful response of the students promises to make necessary several three-week courses during the summer months in order to accommodate the students applying.

The course first set up and successfully conducted in the Summer of 1947 was as follows:

Undergraduate Course

FIRST WEEK

Monday, June 23, 1947:

1:00 - 1:45 P. M.:
Introduction to Course. Orientation to Sanatorium Divisions.

1:45 - 4:45 P. M.:
Diagnosis of Tuberculosis (Case Demonstration).

Tuesday, June 24, 1947:

9:00 - 12:00 Noon:
Laboratory Aids and Techniques in Diagnosis. Demonstration of Laboratory Methods. (Tuberculin Test, Hematology in Tuberculosis).

1:30 - 4:00 P. M.:
Roentgenology (Principles and Method). Fluoroscopy (Principles, Value and Demonstration of Technique). X-ray Classification of Tuberculosis.

4:00 - 5:00 P. M.:
Prophylaxis of Tuberculosis (Illustrated Talk).

Wednesday, June 25, 1947:

9:00 - 11:00 A. M.:
Conference on Sanatorium Admissions (Patient and Film Demonstration. Case Discussion (Diagnosis and Treatment).

11:00 - 12:00 Noon:
National Tuberculosis Association Classification of Extent of Tuberculosis and Clinical Status, (X-ray Demonstration).

1:00 - 4:30 P. M.:
Pathology of Tuberculosis. Pathogenesis of Tuberculosis (Illustrated Talk). Demonstration of Museum Specimens. Performance of Autopsy.

Thursday, June 26, 1947.

9:00 - 9:40 A. M.:
Question and Discussion Period.

9:45 - 11:00 A. M.:
General Treatment of Tuberculosis (Rest, Diet, Heliotherapy, Symptomatic).

11:00 - 12:00 Noon:
X-ray Diagnosis in Tuberculosis (X-ray Demonstration).

1:00 - 5:00 P. M.:
Collapse Therapy in Tuberculosis. Film on Artificial Pneumothorax (Indications, Contra-indications, Technique, Complications). Case Demonstration of Initial Pneumothorax Refills. Film on Bronchography.

Friday, June 27, 1947:

9:00 - 9:40 A. M.:
Question and Discussion Period.

9:40 - 12:00 Noon:
Pneumoperitoneum in Treatment of Tuberculosis. Case Demonstration of Initial Pneumoperitoneum.

1:00 - 3:00 P. M.:
Surgical Collapse Methods in Tuberculosis (Thoracoplasty, Pneumonolyses, Phrenic Operations, etc.). Illustrated Talk.

3:15 - 4:45 P. M.:
X-ray Demonstration of Cases Before and After Surgical Procedures.

Saturday, June 28, 1947:

9:00 - 11:30 A. M.:
Operative Clinic. Demonstration of Phrenic Crush and Intrapleural Pneumonolyses.

11:30 - 12:10 P. M.:
Presentation of Post-Operative Cases (After Pneumonolyses, Thoracoplasty and Phrenic Operation).

1:15 - 4:15 P. M.:
Grand Clinical Conference: Case Presentation and Discussion (Treatment).

SECOND WEEK

Monday, June 30, 1947:

9:00 - 12:00 Noon:
Emergencies in Tuberculosis (Hemorrhage, Spontaneous Pneumothorax, Empyema, Atelectasis). Case and X-ray Demonstrations.

1:00 - 2:00 P. M.:
Prognosis in Tuberculosis.

2:00 - 4:30 P. M.:
Pleural Tuberculosis. Tuberculosis and Diabetes.

Tuesday, July 1, 1947:

9:00 - 11:00 A. M.:
Streptomycin Therapy in Tuberculosis.

11:00 - 12:00 Noon:
Inhalation Therapy in Pulmonary Disease.

1:15 - 4:45 P. M.:
Laryngeal Tuberculosis. Case Demonstrations of Laryngeal Tuberculosis.

Wednesday, July 2, 1947:

9:00 - 12:00 Noon:
Conference on Sanatorium Admissions (Patient and Film Demonstration). Case Discussion (Diagnosis and Treatment).

1:00 - 3:00 P. M.:
Pregnancy in Tuberculosis (Case and X-ray Demonstration).

3:00 - 5:00 P. M.:
Allergy and Immunity in Tuberculosis.

Thursday, July 3, 1947:

9:00 - 10:00 A. M.:
Differential Diagnosis (X-ray Demonstration).

10:00 - 12:15 P. M.:
Differential Diagnosis (X-ray Demonstration).

1:00 - 3:00 P. M.:
Social Aspects in Tuberculosis. Rehabilitation in Tuberculosis. Rehabilitation: Case Conference.

3:00 - 5:00 P. M.:
Public Health in Tuberculosis.

6:30 - 9:30 P. M.:
Differential Diagnosis (X-ray Demonstration).

Saturday, July 5, 1947:

9:00 - 12:00 Noon:
Tracheobronchial Tuberculosis (Illustrated Talk and Moving Pictures). Bronchoscopic Clinic (Case Demonstrations).

THIRD WEEK

Monday, July 7, 1947:

9:00 - 12:00 Noon:
Assignment of Cases to Students. (History Taking and Physical Examination).

1:00 - 1:30 P. M.:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

1:30 - 3:30 P. M.:
Gastrointestinal Tuberculosis (X-ray Demonstration).

3:30 - 5:00 P. M.:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

Tuesday, July 8, 1947:

9:00 - 12:00 Noon:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

1:15 - 4:30 P. M.:
Differential Diagnosis.

Wednesday, July 9, 1947:

9:00 - 12:00 Noon:
Conference on Sanatorium Admissions (Patient and Film Demonstration). Case Discussion (Diagnosis and Treatment).

1:00 - 3:30 P. M.:
Tuberculosis and Lues (Case Demonstration). Dermatology Clinic.

3:30 - 5:00 P. M.:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

Thursday, July 10, 1947:

9:00 - 12:00 Noon:
Ward Rounds (Case Discussion and Physical Diagnosis).

1:00 - 3:30 P. M.:
Genito-urinary Tuberculosis. Illustrated Talk. Film on Nephrectomy. Urology Clinic (Case Presentations).

3:30 - 5:00 P. M.:
Ward Rounds (Case Discussion and Physical Diagnosis).

Friday, July 11, 1947:

9:00 - 12:00 Noon:
Ward Rounds (Case Discussion and Physical Diagnosis). Assignment of Cases to Students (History Taking, Physical Examination).

1:00 - 4:15 P. M.:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

Saturday, July 12, 1947:

9:00 - 10:45 A. M.:
Ward Rounds (Case Discussion and Physical Diagnosis).

10:45 - 12:00 Noon:
Differential Diagnosis.

1:30 - 4:30 P. M.:
E. N. T. Clinic Case Presentations of Laryngeal Tuberculosis and Ear Tuberculosis.

The undergraduate course having been launched, a postgraduate course was established in order to make available to the practicing physician similar opportunities for study. The increase in tuberculosis to epidemic proportion at a time when educational facilities and medical personnel are at the lowest ebb in war-torn Europe and Asia has made this country the hope of the world. Inquiries concerning the course have been received from Europe, India, China and South America. All these pertained to the possibilities of postgraduate instruction in Diseases of the Chest. All applications were referred to the Dean of the New York Medical College within whose jurisdiction lay the acceptance of the students. As in the case of the senior students, arrangements were made to house postgraduate students at the Sanatorium Staff house. With experience gained by the first course, certain changes were made in the curriculum and the course presented was as follows:

Postgraduate Course

FIRST WEEK

Monday, October 20, 1947:

9:00 - 10:30 A. M.:
Epidemiology.

10:30 - 12:00 Noon:
Laboratory Aids and Techniques in Diagnosis.

1:00 - 4:00 P. M.:
Demonstration of Laboratory Methods (Tuberculin Testing, Hematology in Tuberculosis).

4:00 - 5:00 P. M.:
Prophylaxis of Tuberculosis (Illustrated Talk).

Tuesday, October 21, 1947:

9:00 - 12:00 Noon:
Pathology of Tuberculosis. Pathogenesis of Tuberculosis (Illustrated Talk). Demonstration of Museum Specimens.

1:00 - 4:00 P. M.:
X-ray Diagnosis of Pulmonary Diseases.

4:00 - 5:00 P M.:
National Tuberculosis Association Classification of Tuberculosis in Relation to Pulmonary Involvement and Clinical Manifestations. (X-ray Demonstration).

Wednesday, October 22, 1947:

9:00 - 12:00 Noon:
Physiology of Pulmonary Diseases.

1:00 - 3:30 P. M.:
Diagnosis of Tuberculosis: Clinical Methods (Case Demonstration).

3:30 - 5:00 P. M.:
Conference on Sanatorium Admissions.

Thursday, October 23, 1947:

9:00 - 9:30 A. M.:
Question and Discussion Period.

9:30 - 12:00 Noon:
General Treatment of Tuberculosis (Rest, Diet, Heliotherapy, Symptomatic).

1:00 - 5:00 P. M.:
Collapse Therapy in Tuberculosis. Sound Film on Artificial Pneumothorax (Indications, Contra-Indications, Technique, Complications). Case Demonstration of Initial Pneumothorax Refills. Sound Film on Bronchography.

Friday, October 24, 1947:

9:00 - 9:30 A. M.:
Question and Discussion Period.

9:30 - 12:00 Noon:
Pneumoperitoneum in Treatment of Tuberculosis. Case Demonstration of Initial Pneumoperitoneum.

1:00 - 3:00 P .M.:
Allergy in Pulmonary Disease.

3:00 - 5:00 P. M.:
Pulmonary Anatomy, Pulmonary Segments and Broncho-pulmonary Disease.

Saturday, October 25, 1947:

9:00 - 12:00 Noon:
Operative Clinic Demonstration of Phrenic Crush and Intrapleural Pneumonolyses.

1:15 - 4:15 P. M.:
Grand Clinical Conference: Case Presentation and Discussion.

SECOND WEEK

Monday, October 27, 1947:

9:00 - 11:00 A. M.:
Emergencies in Tuberculosis (Hemoptysis, Spontaneous Pneumothorax, Empyema, Atelectasis, etc.). Case and X-ray Demonstrations.

11:00 - 12:00 Noon:
Prognosis in Tuberculosis.

1:00 - 3:00 P. M.:
The Pleura in Tuberculosis.

3:00 - 5:00 P. M.:
Diabetes and Tuberculosis.

Tuesday, October 28, 1947:

9:00 - 12:00 Noon:
Laryngeal Tuberculosis. Etiology, Symptomatology. Clinical Course. Differential Diagnosis. Therapy.

1:15 - 4:45 P. M.:
Laryngeal Tuberculosis. Case Demonstrations.

Wednesday, October 29, 1947:

9:00 - 12:00 Noon:
Conference on Sanatorium Admissions. (Patient and Film Demonstration). Case Discussion (Diagnosis and Treatment).

1:00 - 3:00 P. M.:
Pregnancy in Tuberculosis (Case and X-ray Demonstration).

3:00 - 5:00 P. M.:
Genito-urinary Tuberculosis. Case Presentation.

Thursday, October 30, 1947:

9:00 - 12:00 Noon:
Differential Diagnosis in Pulmonary Diseases (X-ray Demonstration).

1:00 - 3:00 P. M.:
Social Aspects of Tuberculosis. Rehabilitation in Tuberculosis. Rehabilitation Case Conference.

3:00 - 5:00 P. M.:
The Role of the Public Health Worker in Tuberculosis. Case Finding and Follow-Up.

Friday, October 31, 1947:

9:00 - 10:30 A. M.:
Allergy and Immunity in Tuberculosis.

10:30 - 12:00 Noon:
Cardiac Factors in Pulmonary Disease.

1:00 - 3:00 P. M.:
The Surgical Approach to the Therapy of Tuberculosis (Thoracoplasty, Pneumonolyses, Phrenic Operations, etc.).

Saturday, November 1, 1947:

9:00 - 12:00 Noon:
Tracheobronchial Tuberculosis (Illustrated Talk and Motion Pictures). Bronchoscopic Clinic (Case Demonstrations).

1:15 - 4:15 P. M.:
Grand Clinical Conference: Case Presentation and Discussion.

THIRD WEEK

Monday, November 3, 1947:

9:00 - 12:00 Noon:
Assignment of Cases to Students (History Taking and Physical Examinations).

1:00 - 3:00 P. M.:
Gastro-Intestinal Tuberculosis (X-ray Demonstration).

3:00 - 5:00 P. M.:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

Tuesday, November 4, 1947:

9:00 - 12:00 Noon:
Antibiotic Therapy. Streptomycin Therapy in Tuberculosis: Technique, Evaluation. Aerosol Therapy in Pulmonary Diseases. Experience with Promin, Penicillin and Streptomycin.

1:15 - 4:30 P. M.:
Differential Diagnosis in Pulmonary Diseases.

Wednesday, November 5, 1947:

9:00 - 12:00 Noon:
Conference on Sanatorium Admissions. (Patient and Film Demonstration). Case Discussion (Diagnosis and Treatment).

1:00 - 3:30 P. M.:
Tuberculosis and Lues (Case Demonstration). Dermatology Clinic.

3:30 - 5:00 P. M.:
Ward Rounds (Discussion and Examination of Cases Worked Up By Students).

Thursday, November 6, 1947:

9:00 - 12:00 Noon:
Ward Rounds (Case Discussion and Physical Diagnosis).

1:00 - 2:30 P. M.:
Industrial Aspects of Tuberculosis: Occupational, Environment, Trauma.

2:30 - 5:00 P. M.:
Fungus Diseases.

Friday, November 7, 1947:

9:00 - 12:00 Noon:
Ward Rounds (Case Discussion and Physical Diagnosis). Assignment of Cases to Students (History Taking, Physical Examination).

1:00 - 3:00 P. M.:
Psychosomatic Factors in Tuberculosis.

3:00 - 5:00 P. M.:
Ward Rounds (Case Discussion and Physical Diagnosis).

Saturday, November 8, 1947:

9:00 - 12:00 Noon:
Surgical Clinic.

1:15 - 4:15 P. M.:
Grand Clinical Conference: Case Presentation and Discussion.

The program outlined is not inflexible and will be modified as necessary. The aim is to present not dry didactic lectures but to associate in the student's mind all the phases and aspects of the disease, physical, psychological and social as applied to the actual patient.

There is no doubt that such instruction would be best given in a general hospital where the student could observe tuberculosis along with other diseases as a long term project as part of his general clinical studies. Unfortunately, few general hospitals have adequate facilities for the care of tuberculosis and the case that is seen is discovered accidently or is admitted as an emergency. In most cases, these hospitals become way stations or transfer points where the patient lies awaiting admittance to a tuberculosis hospital or sanatorium. Rarely are these cases treated during these often critical periods and more rarely are they utilized for teaching purposes. Until the general hospital takes a more modern and progressive view of the disease and assumes its proper place in the care and teaching of tuberculosis, we must rely upon the sanatorium and tuberculosis hospital.

The Municipal Sanatorium is ideally fitted for this purpose because of the early phases of the disease that are seen. The applicability and effectiveness of therapy can be better demonstrated to students when they are shown early or relatively early cases. Students and practitioners tend to be overwhelmed and confirmed in their belief in the hopelessness of the disease when they are confronted by far-advanced cases, large cavities and incurable chronics. To counteract this view the student should have the opportunity of observing the disease in all its phases.

Following the lectures on the various subjects listed in the schedule, the students received practical bedside training in the application of the principles of diagnosis and therapy. Experience in actual therapy was made available, specifically in the technique of collapse measures, such as pneumothorax and pneumoperitoneum. Surgical and Medical Conferences were attended where

a thorough discussion was held on the cases that had been observed and studied by the students.

The entire treatment of tuberculosis loses all focus and meaning unless the patient can be returned as a useful member of society with all the psychological implications of that phrase. The Municipal Sanatorium is well aware of that factor in the treatment of tuberculosis and has set up a coordinated occupational therapy and rehabilitation program.

The students observed and were impressed with the importance of such a program. In so doing, they ceased considering the tuberculous patient as a case and began to consider each patient as an individual to be integrated into his or her environment in as normal or usual a manner as was compatible with his disease process.

The over-all picture of tuberculosis as a Public Health problem to be combatted not only locally but throughout the nation was presented to the students. Techniques of case history and follow up, principles of hygiene, and the role of hospital and Department of Health clinics were included in order that the student might understand and appreciate the machinery that has been set up to cope with the disease outside the microcosm of the hospital and sanatorium.

SUMMARY

It is our hope that eventually the teaching of tuberculosis will accompany the student throughout the four years of his medical school, not as an elective, but as a required course correlated with all his other subjects. In this instance, familiarity will breed not contempt but knowledge of, and respect for, a disease that thrives on ignorance.

The success of the courses given was due directly to the enthusiasm and wholehearted cooperation of the Dean and Medical Board of the New York Medical College and the Medical Staff of the Municipal Tuberculosis Sanatorium.

RESUMEN

Abrigamos la esperanza de que con el tiempo la enseñanza de la tuberculosis acompañará al estudiante durante sus cuatro años en la escuela de medicina, no como una materia electiva sino obligatoria y correlacionada con todas las otras materias. En este caso la familiaridad no engendrará menosprecio sino más bien el conocimiento y respeto de una enfermedad que florece en la ignorancia.

El buen éxito de los cursos de instrucción se debió directamente al entusiasmo y activa cooperación del Decano y Junta Médica del Colegio Médico de Nueva York y el Claustro Médico del Sanatorio Municipal para Tuberculosos.

Technique of Caulfeild's Inhibitive Test also of Tuberculo-Complement Fixation Test*

For Serological Anticipation of Tuberculous Disease

(With Data Supplemental to Publication of 1925)

M. FLORENCE MACLENNAN, B.A., Serologist
Toronto, Canada

Preface (a):

"The Inhibitive reaction of Caulfeild is specific for tuberculosis" (A.C.N.). We consider both the Inhibitive and Fixation reactions to be specific for this disease.

The fifty page symposium "Foreseeing and Forestalling Tuberculosis* (Twenty Years' Observations on the Approach of Tuberculous Disease)," by Ogden, Anglin, Kruger, Norwich, O'Sullivan, Macintyre, and sixteen collaborators, appeared in "Diseases of the Chest" of July-August 1946.† Immediately, enquiries concerning the latest technique of the tests came from abroad as well as from America. Possibly others were already proceeding with the tests, employing the technique as given in a former symposium, "The Tuberculo-Complement-Fixation and Inhibitive Tests," by Caulfeild, A. H. W., et al, in the "American Review of Tuberculosis," XI:508, 1925. When our recent Director of Laboratories, Dr. A. C. Norwich, was consulted, he advised that our Chief Serologist, Miss M. F. Maclennan, be asked to re-write the latest technique. This is presented herewith following the next several introductory paragraphs.

The use and value of these tests are given in the following excerpts from the text of the symposium:

"We know that a positive tuberculin skin test signifies that tuberculous infection has taken place. If, months or years later, symptoms appear, or x-ray films demonstrate a lesion, disease has already developed. Are there any means by which in this *blackout period* we may be informed of such serious transition from infection to disease before it actually happens? We believe that serial serological tests indicate that the infection is no longer dormant and that a transitional stage has been reached which, if unrecognized and untreated will lead to active clinical tuberculosis clearly demonstrable by routine methods" (G.C.A.).

---

*Presented at the 7th Annual Meeting of the American College of Chest Physicians, Cleveland, Ohio, May 31, 1941, by W. E. Ogden, M.D., F.C.C.P.
†Limited number of reprints available.

"We have presented evidence that by means of serological tests it may be possible to diagnose tuberculosis six months to two years before the appearance of clinical signs and symptoms, and that by the addition of fractional daily amounts of rest during this pre-clinical stage, the onset of manifest disease may be prevented. As the average incubation period of tuberculosis is three to five years, it should not be hard to believe that immunological reactions occurring in the body during that time are reflected in the serum."

"Groups most easily tested and supervised are, nurses in training, and tuberculosis contacts." It would be logical to test all tuberculin positive individuals as they have been contacts. "In our hospital School for Nurses, we do not wait for an annual x-ray film to demonstrate a lesion in its early stage, when, of course, it is too late for prevention. We are anticipating clinical or x-ray evidence of disease by biological tests and precluding it by extra hygienic care." "In 20 years regular testing of over 2,500 tuberculosis contacts and nurses, only two cases have developed without previous serological warnings, and none where the prescribed extra rest has been taken." The greater part of the clinical work has been done at the Toronto Western Hospital.

Another problem-type of case which we have been solving by serology, is the one with the "spot" found incidentally by x-ray, and without symptoms. "If silent minimal tuberculous lesions found by mass x-ray survey, appear possibly healed, and if they give normal serum reactions, the patient is allowed to remain at work, pending further serology. If the tests change and indicate biological tuberculosis and therefore potential clinical disease, the individual is disqualified for work and rest is ordered; if the tests remain normal, his work is not interrupted."

W. E. Ogden, E.D., M.D., F.A.C.P., F.C.C.P.
Director of Chest Clinic, Toronto Western Hospital.

216 Medical Arts Building,
Toronto, Canada.

Preface (b):

Having observed, over a number of years, the results in many thousands of tests, I am firmly convinced of their reliability and value to the painstaking and patient clinician for diagnostic and prognostic purposes in biological (pre-clinical) and in clinical pulmonary tuberculosis.

Early in the serological investigation of tuberculosis by the late Doctor A. H. W. Caulfeild, Miss Maclennan became one of his technicians and for over twenty-five years, has most conscientiously and effectively toiled in this field. "The work of

Science is to substitute facts for appearances, and demonstrations for impressions" (Ruskin). We are convinced that, above all others, she is eminently qualified to make this record.

Arthur C. Norwich, M.B.,
Recent Director of Laboratories, D. V. A.

23 Austin Crescent,
Toronto, Canada.

Caulfeild's Inhibitive Test — Technique

Part I. *Inhibitive Test:*

In complement fixation tests the antigens are usually in dilutions which are not anticomplementary, and the positiveness of results is in direct ratio to the amount of complement fixed after incubation with antigen and antibody. In Caulfeild's Inhibitive Test, this technique and interpretation are reversed. The antigen is used in dilutions which *are* anticomplementary, and the positiveness of results is in direct ratio to the amount of complement remaining "free" after incubation with antigen and antibody. It is not a "Fixation" antigen in the accepted meaning of that term.

The reaction between Inhibitive Antigen and a positive serum apparently takes place before addition of complement, thus leaving the latter "free" until the haemolytic system is added. This property of a positive serum, designated "Inhibitin" by Caulfeild, counteracts the anticomplementary factor in the antigen. If the serum being tested does not lessen the anticomplementary strength of the antigen, complement when added will, of course, be absorbed by the antigen and haemolysis will not result after addition of the haemolytic system. It would seem that such an antigen might be adapted to a precipitation test, but so far attempts to do so here have not been successful.

Points stressed for accuracy of results (details given later):

1) Buffered saline must be used in order to bring all the reagents as nearly as possible to pH7. Acidity will cause irregularities and false positives.

2) Sera to be tested must not remain on clot at room temperature longer than 24 hours, nor on clot in refrigerator more than 36 hours.

3) Sera held over from one test to the next as controls for Inhibitive test must be tightly corked to prevent evaporation, and kept in refrigerator.

4) Anti-sheep cell haemolysin must be accurately controlled, both by titration and by removal from the sera by absorption with sheep cells. The latter has been found neither necessary nor desirable for the fixation test with its overnight incubation.

5) Using complement only from pre-tested guinea pigs will prevent many unsatisfactory tests.

6) When haemolysin and sheep cells are combined for haemolytic system, the mixing should be done quickly and just previous to use, otherwise agglutinins will interfere with the action of the complement.

Equipment required: Incubator for growing tubercle bacilli, waterbath 37.5° C. and Centrifuge.

Glassware: Test tubes for blood specimens and sera: ½" x 4".

For diluting sera: Standard Kolmer Wassermann tubes.

For final test: ⅜" x 3" (if "micro" technique used).

Note: Previous to 1939, the last mentioned tubes were imported from Europe. It has been found that those purchased since that date, made of American glass, were unsatisfactory for use with Inhibitive antigen (causing considerable interference with the action of the complement) until they had been repeatedly cleansed and resterilized in hot air oven at 160° C. Allowing them to remain in cleaning fluid (sulphuric acid and pot. bichromate) was not effective in removing the substance causing trouble. This interference with action of complement was noticeable only to a slight degree in the Fixation Test.

Pipettes: For diluting and pipetting sera, preferably 0.5 cc. to tip.

All glassware should be very thoroughly rinsed after cleansing to remove any trace of soap, and sterilized. Here again it should be noted that some of the newer cleansing preparations have not been satisfactory for glassware used in this test.

Tubercle Bacilli for Antigens: (1) For Inhibitive Antigen: Human tubercle bacilli growing *rapidly* on 5 per cent glycerine beef or veal, peptone or trypsin broth, pH7.4 to 7.6, temperature 38 to 39° C. for 5 weeks. (Flat-sided, quart size flasks with about 150 cc. broth in each were found satisfactory). At end of 5 weeks flasks are placed, upright, in Arnold sterilizer for 45 to 60 minutes, allowed to cool at room temperature, contents then filtered through rather coarse filter paper, and, while tubercle bacilli are still in filter paper, rinsed once with buffered saline, then dried in incubator, 38 to 39° C. by placing the filter paper containing tubercle bacilli in a wire basket. When thoroughly dry, store in glass containers in dry place.

Note: Tubercle bacilli grown on synthetic medium have not been found suitable for Inhibitive antigen, probably due to lack of lipoids, but they are satisfactory for Fixation antigen.

Saline Solution: 0.9 per cent NaCl in distilled water, buffered to pH7 (or very slightly below). We have found secondary sodium phosphate Na_2 H P O_4, dibasic, and primary potassium phosphate K H_2 P O_4 monobasic (Clark's "Determination of Hydrogen Ions,"

Soerensen's Phosphate Mixtures, table 27, p. 114) the most satisfactory. Allowance is made for the buffer solution being one half isotonic.

Quantity for 1 liter only:
Stock solution of buffers:

Pot. Phos.: 0.908 gm. in 100 cc. distilled water.

Sod. Phos.: (dried for two weeks before using)
2.375 gm. in 200 cc. distilled water.

To 900 cc. distilled water add NaCl	8.55 gm.
Stock Solution Pot. Phos.	30 cc.
Stock Solution Sod. Phos.	70 cc.

Sterilize in autoclave or Arnold.

Guinea pigs: Only normal pigs are used and these are previously tested in lots of 12 by withdrawing about 4 cc. samples of blood from the heart. Only those are used which have a sufficiently high titre of complement (1 unit not less than 1:40), contain only a negligible amount of natural anti-sheep cell haemolysin, if any, and are not sensitive to the antigens. Fresh complement should be obtained for each test, although any remaining over may be used within two or three days if kept frozen in refrigerator, diluted 1:10 with buffered saline solution.

Preparation of sera: After clots are separated, centrifuge about 1400 R.P.M. for 20 minutes. As mentioned before, sera should not be left on clots longer than 24 hours at room temperature, nor on clots, more than 36 hours when in refrigerator.

Pipette only clear supernatant serum from each specimen into 3 tubes (½" x 4") as follows: (1) 0.45 cc. (2) 0.45 cc. (3) Remainder of clear serum for fixation test. Inactivate 30 minutes at 56° C. Tubes are tightly corked and kept in refrigerator as controls for next Inhibitive test. When there are intervals of only two or three days between tests, sera kept thus will be found satisfactory. The other tubes are also kept in refrigerator, plugged with cotton.

Removal of Natural Anti-sheep cell Haemolysin from sera used for Inhibitive test: On the morning of the test, add 2 drops of washed, packed sheep cells to each of the plugged tubes containing 0.45 cc. serum, shake to mix, allow to stand at room temperature 15 to 20 minutes (preferably not longer because of tendency to become anticomplementary), centrifuge 30 minutes about 1400 R.P.M.

Diluting sera: While titrations are being incubated, pipette 0.1 cc. from each specimen of serum (0.5 cc. pipette) into Standard Wassermann size tube, and add 0.9 cc. saline solution with a 5 cc. pipette, separate racks being used for the fixation serum dilutions, which have not had sheep cells added.

Sheep Cells: Defibrinate with glass beads (This was found pre-

ferable to the use of sodium citrate), and wash four times with buffered saline, centrifuging 15 minutes the last time.

Inhibitive Antigen: Extract in incubator 38 to 39° C. two grams dried, human tubercle bacilli (previously broken into fine granules with a pestle) with 100 cc. equal quantities of absolute ethyl alcohol and ether (for anaesthesia), the latter from *copperlined* container, for 4 weeks in glass stoppered bottle. Shake bottle daily during this period sufficiently to re-suspend tubercle.

At the end of four weeks, pipette the extract into two 50 cc. tubes (Roseneau centrifuge tubes are convenient), centrifuge at high speed for 30 minutes, then carefully decant or pipette supernatant into a porcelain evaporating dish 150 cc. capacity and place in incubator 38 to 39° C. until all liquid has evaporated—24 to 36 hours. Re-dissolve the deposit remaining by holding the evaporating dish partly submerged in water bath at 56° C. and rinsing it into a small, glass stoppered bottle with small quantities of the 50-50 alcohol-ether, using a 2 cc. or 5 cc. pipette (total of approximately 10 cc. for this amount of extract). Use only sufficient alcohol-ether to cause the cloudy solution in bottle to just clear or become opalescent when the bottle is held in water bath at 56° C. for one or two minutes. One might consider it a saturated lipoidal solution. Store in dark at room temperature.

Alternative, original method: After evaporation, rinse deposit into small bottle with sufficient alcohol-ether to make a 2 per cent solution. Inhibitive Antigen should remain stable for a month. If it becomes too anti-complementary before this time, a small quantity of alcohol-ether may be added to compensate for evaporation. This extract is ready for use after standing a few days.

Dilution of Inhibitive Antigen for each day's Test: Hold the small bottle of antigen in water bath at 56° C. until solution clears. Using a slightly warm 0.5 or 1.0 cc. pipette, measure the amount required for all the dilutions into a warm tube. While slowly revolving tube, add, with a 5 cc. or 10 cc. pipette, sufficient buffered saline, previously heated in small flask to about 60° C., to give required dilution. Mix well. For the second dilution, one half strength of first, transfer part of this first dilution to another warm tube and add an equal quantity of heated saline solution and from this latter dilution make the third dilution, one-half strength of second, using the heated saline solution throughout. If it is found necessary after titration to alter dilutions, commence again with the undiluted extract instead of trying to modify dilutions already made. Allow antigen dilutions to cool at room temperature before using. The anti-complementary dilutions required (ratio 1 : ½ : ¼) are often found to approximate 1:40, 1:80, 1:160, but may vary considerably.

Daily titrations:

(1) Haemolysin: (Supposing approximate titre to be 1:1000 equals 2 units, as previously determined by any standard method). Place 5 (⅜" x 3") tubes in a rack.

Tubes for Inh. Haemolysin	*1*	*2*	
Buffered Saline Solution	0.2 cc.	0.2 cc.	
Complement 1:20	0.1 cc.	0.1 cc.	
For Fix'n Haemolysin	*1*	*2*	*3*
Buffered Saline Solution	0.2 cc.	0.2 cc.	0.2 cc.
Complement 1:30	0.1 cc.	0.1 cc.	0.1 cc.
Incubate one hour in water bath at 37.5° C.			

Just before the end of this period, make up small amounts of haemolysin and sheep cell mixtures (Standard Kolmer Wassermann tubes are convenient size for this) as follows:

Tubes:	*1*	*2*	*3*
Haemolysin (1:1000)	0.25 cc.	0.25 cc.	0.25 cc.
Saline Solution	0.25 cc.	0.5 cc.	0.75 cc.
Dilutions are now	1:2000	1:3000	1:4000

Mix, and discard 0.25 cc. from second and 0.5 cc. from third tube. To each tube add, mixing quickly, 0.5 cc. sheep cell suspension 1:20, thus obtaining three "mixtures" containing 1, 1/3 and ¼ units, approximately, for fixation test. To the three tubes for fixation haemolysin titration, add 0.1 cc. of each of these three "mixtures." To the two tubes for Inhibitive Haemolysin titration, add 0.1 cc. of mixtures containing 1/3 and ¼ units respectively.

Re-incubate 30 minutes and read. If the unit of haemolysin (1:1000, as previously determined) is correct with this particular complement, the readings will be, for Inhibitive haemolysin titration: CH, ACH and for Fix'n Haemolysin titration, CH, ACH, PH. As barely two units of haemolysin are used for the Inhibitive test, the dilution required according to above example would be 1:2000. As two or more units are used in the Fix'n test, the dilution would be 1:1000. This is actually more than two units, since, in order to save time, the incubation period for Inhibitive complement titration is used for both these titrations, whereas with incubation period for the complement fixation titration less than this amount of haemolysin would be absorbed. The arbitrary complement dilutions of 1:20 for Inhibitive and 1:30 for Fixation haemolysin

titrations are chosen because they approximate those usually required in the final tests. Daily titration to determine dilutions of Inhibitive Antigen and Complement. (Supposing anti-complementary dilutions of antigen are 1:40, 1:80, 1:160).

Tubes, 1st row:	*1*	*2*	*3*
Buffered Saline Solution	0.1 cc.	0.1 cc.	0.1 cc.
Inh. Ant. 1:40	0.1 cc.	0.1 cc.	0.1 cc.
Complement	0.1 cc. (1:10)	0.1 cc. (1:20)	0.1 cc. (1:30)

2nd row: Same as above except that antigen dilution is 1:80.
3rd row: Same as above except that antigen dilution is 1:160.

It is advisable to set up 3rd row in duplicate.

Complement dilutions may be extended in one row up to 1:70, using 0.1 cc. of each dilution, 0.2 cc. of saline solution and omitting antigen, to determine one unit.

Incubate in waterbath at 37.5° C. for one hour.

Add 0.1 cc. haemolytic system (mixture of equal quantities sheep cells 1:20 and dilution of haemolysin equivalent to almost two units according to the preliminary titration). A small quantity should be prepared just before needed. After addition of haemolytic system, incubate ½ hour and read.

The strength of complement to be used in the final test is that which will produce just the commencement of haemolysis in the weakest dilution of antigen. For example:

Complement:	*1:10*	*1:20*	*1:30*	*1:40*	*1:50*	*1:60*	*1:70*	*1:80*
1st row (Antigen 1:40)	NH	NH	NH					
2nd row (Antigen 1:80)	PH	NH	NH					
3rd row (Antigen 1:160)	CH	*PH*	NH					
Saline control				CH	CH	*CH*	ACH	PH

If the second tube in antigen dilution 1:160 shows haemolysis which is just barely discernible, complement dilution 1:20 would be indicated, i.e.: three units according to the saline control in above example. Two and a half units or more of complement should be used. Thus in the final test the weakest dilution of antigen in control tube will be almost completely anti-complementary.

Final Inhibitive Test: (A control rack with several sera from

previous day's test, and antigen controls for each dilution, is included). Racks are shaken after addition of each reagent.

Four tubes for each serum:	*1*	*2*	*3*	*4*
Serum (1:10)	0.1 cc.	0.1 cc.	0.1 cc.	0.2 cc.
Antigen	0.1 cc. (1:40)	0.1 cc. (1:80)	0.1 cc. (1:160)	omit
Incubate in waterbath at 37.5° C. for 20 minutes.				

Add 0.1 cc. complement throughout according to strength determined by titration and re-incubate 1 hour in water bath at 37.5° C.

Add 0.1 cc. haemolytic system (combined just before required) and re-incubate until negative and positive controls show approximately the same degree of haemolysis as in previous test and antigen controls are NH, NH, PH.

As it has sometimes been difficult (due to the variability of complement and due to the antigen becoming slightly more anticomplementary between time of titration and use in test) to determine the correct dilution of complement, it has been found very helpful to first set up one rack with 4 or 5 control sera from the previous day's test and the same number from the day's specimens, and have it precede the regular test by about half an hour. If, during the final incubation period of this "test" rack it is found that too much or too little complement had been used, the racks for the main test could then be incubated a longer or shorter period before adding haemolytic system, and also the amount of haemolysin could be changed if necessary, thus making adjustment before the final incubation period.

Addition of Haemolytic System to Inhibitive Test: Add first to rack containing control sera and antigen controls, noting time, then add to remaining racks singly or by two's, noting time. In order to obtain uniformity of results, no definite time is stipulated for this final incubation. When the antigen controls in the first rack show NH, NH PH (?) and the repeated control sera show approximately the same degree of haemolysis as in the previous day's test, remove this control rack, and allow the remaining racks the same length of time in water bath—usually 30 to 60 minutes.

Readings are made at once and also after racks have been in refrigerator overnight.

Strength of a new antigen is determined simply by comparing results of a few sera with those obtained with the antigen in use.

Interpretation of results: The average serum from a clinically nontuberculous adult will cause partial or complete haemolysis

in the tube containing the least anti-complementary dilution of antigen, but not in those containing the more anti-complementary dilutions.

Terminology used in reporting readings: (Occasionally, slight modifications have to be made if the antigen proves to be more or less anti-complementary than indicated by preliminary titration): NH is expressed by "4," PH by "3," PH plus by "2," ACH by "1," CH by "0."

Readings	*Original Terminology*	*Later Terminology*
1000	First class	4 plus plus
2000-3000	2nd plus	4 plus
4000-4100	2nd class	3 plus
42+00	2nd minus	2 plus
4200	3rd plus	1 plus
4300-4420	3rd class	negative
4430-4440	Indifferent	minus

The "Indifferent" result, where the antigen has not been acted on by the serum to any appreciable extent, is noticed more frequently with sera from infants than from adults. It has been considered an unfavorable indication when occurring with sera from clinically tuberculous adults. The "Third Class" or "Negative" is the average result shown by clinically normal adults. With reference to these so called "normal" results, the following is quoted from reprint of Caulfeild's article in "The American Review of Tuberculosis," 11:6, August, 1925:

"If obtained in the tuberculous with, for instance, fever and malaise, we believe the prognosis to be poor, although it has the reverse significance if the case is arrested, is without fever and is doing well."

With reference to positive results, (i.e., second class or three plus) the following is quoted from the same article: . . . . (this) "serological finding indicates biological activity and likely therefore in the majority of cases to be clinically evident later."

The very strongly positive results (4 plus and 4 plus plus) are obtained rather infrequently.

Of 800 normal guinea pigs tested with Caulfeild's Inhibitive antigen over a period of ten years, three showed a 2 plus and one a 3 plus reaction.

Positive Inhibitive reactions have been frequently observed in cases of carcinoma (diagnoses from autopsy records).

Other lipoidal extracts from tubercle have been tested as "inhib-

itive" antigens and results compared with those of Caulfeild's. Of these, an acetone extract of tubercle, and an alcohol, ether, acetone extract seemed to parallel most closely the results obtained with the alcohol-ether extract. Some antigens tested with this technique were unstable, others non-specific, as in the following examples:

Alcohol-ether extract of tubercle bacilli previously extracted with toluol for nine days;—less stable and results positive with normal guinea pig sera.

Toluol extract of tubercle bacilli evaporated and sediment resuspended with alcohol-ether:—results positive with normal guinea pig sera.

Alcohol-ether extract of B. diphtheriae:—positive results with normal guinea pig sera; antigen itself haemolytic for sheep cells when used in dilutions required by inhibitive technique.

Alcohol-ether extract of B. smegmatis:—positive results with normal guinea pig sera.

A noticeable similarity in many of the results obtained with alcohol-ether extracts of tubercle, diphtheria and smegma bacilli would indicate some common factor.

Kolmer's Wassermann Antigen—Reversed readings in antigen controls, results unlike those obtained with alcohol-ether extract of tubercle bacilli.

Cholesterin—reversed readings in antigen controls. (It may be of interest to note here that a 1:400 saline dilution of a 2 per cent suspension of cholesterin in alcohol, the percentage used in Wassermann Antigens, also resulted in reversed readings when used in place of antigen with the routine Wassermann technique, which would suggest the possibility that this reagent might be responsible for reversed readings, other than those caused by natural anti-sheep cell haemolysin, occurring in the Wassermann test).

A small quantity of *histamine* added to sera did not alter inhibitive reaction.

Tests were made to determine whether more positive Inhibitive reactions occurred with sera containing an excessive amount of natural anti-sheep cell haemolysin (i.e., before absorption with sheep cells). There was found to be no parallelism.

The late Dr. W. Ray Hodge, in an article published in the Journal of Immunology, Vol. VII, No. 3, May 1922, stated that the "substances responsible for the inhibitive reaction of Caulfeild are contained almost wholly in the euglobulin fraction of the serum." This conclusion was based on tests with the euglobulin fraction of sera precipitated with carbon dioxide.

During the past year, total protein, globulin and albumin estimations were made in the chemical laboratory* on a few sera sent from the chest clinic for serological tests, to determine whether "Inhibitin" might be related to an increase in any one of these fractions. Although, unfortunately, it was not possible to have many estimations made, the percentages in Table I indicate that sera showing positive Inhibitive reactions are not limited to those which are above or below the normal range in any one of these fractions. The twenty-two globulin and albumin estimations were made on the same sera, and since they all happened to be within the normal range, the percentages are the same for both.

A record was made of 283 sedimentation rates on sera (from male, chest clinic patients) on which Inhibitive tests were made at the same time. The figures given in Table II indicate a definite divergence in results between these two tests.

Part II. *Tuberculo-Complement Fixation Test:*

Antigen:—a modification of that described in Petroff's "Studies of Humoral Antibodies in Tuberculosis," as follows:—Grind 0.5 grams dried tubercle bacilli, human type, plus an equal quantity

*Courtesy of Wm. C. Arrowsmith.

TABLE I

Total proteins (Van Slyke Method)

(Normal range 6.5 to 7.5 grams per cent)

	Normal Inhibitive Per cent	Borderline Inhibitive Per cent	Positive Inhibitive Per cent
34 sera within normal total protein range:	17 (50)	8 (23.5)	9 (26.5)
9 sera above normal total protein range:	3 (33.3)	0	6 (66.7)

Globulin and *Albumin*

(Normal, 1.2 to 2.3 gm. per cent) (Normal 4.2 to 6.7 gm. per cent)

	Normal Inhibitive Per cent	Borderline Inhibitive Per cent	Positive Inhibitive Per cent
22 sera all within normal range:	12 (54.5)	6 (27.3)	4 (18.2)

of sterile, ground glass in mortar with a small quantity of toluol for 2 to 3 hours; add about 20 cc. toluol and incubate in glass stoppered bottle, about 38° C. for 5 to 6 days. Replace in mortar and grind again until toluol is evaporated. Combine 12½ cc. glycerine with 37½ cc. sterile distilled water, add small quantity to tubercle bacilli in mortar and grind 2 to 3 hours, then rinse with remaining glycerine and water into a small, pyrex flask (150 cc. capacity). Simmer this emulsion under a reflux condenser for one hour, being careful not to allow it to boil. Allow antigen to remain in flask overnight so that the large particles will settle out, then pipette into small bottles and store in refrigerator. This antigen remains stable for a year.

(A more sensitive fixation antigen is obtained from an acetone precipitate of filtrate from tubercle bacilli grown on broth 5 to 6 weeks. An equal quantity of acetone is added to the filtrate, allowed to remain at room temperature two hours, centrifuged, and precipitate re-suspended in sufficient distilled water to make up the original volume of filtrate, with addition of NaCl to make isotonic. By using half glycerine and half distilled water the antigen is made more stable. This antigen has not been used routinely).

Filtrate from broth culture of B. diptheriae precipitated by above method does not cause fixation when combined with tuberculous sera, although the organism itself used as an antigen (Petroff's

TABLE II

Sedimentation Rates

	Normal Inhibitive Per cent	Borderline Inhibitive Per cent	Positive Inhibitive Per cent
245 sera with drop or less than 15 mm. in first hour:	158 (64.5)	46 (18.8)	41 (16.7)
23 sera with sedimentation rate 15-30 mm. in first hour:	7 (30.4)	8 (34.8)	8 (34.8)
11 sera with rate 30-50 mm. in first hour:	2 (18)	1 (9)	8 (73)
4 sera, rate 50-100 mm. in first hour:	(1 Indifferent reaction, 25 per cent)	0	3 (75)

Method) gives results very similar to those obtained with tubercle bacilli.

Titration of Complement:

1st row of tubes	*1*	*2*	*3*	*4*	*5*	*6*
Complement dilutions	0.1 cc. (1:40)	0.1 cc. (1:50)	0.1 cc. (1:60)	0.1 cc. (1:70)	0.1 cc. (1:80)	0.1 cc. (1:90)
Antigen (usually about 1:150)	0.1 cc.	0.1 cc.	0.1 cc.	0.1 cc.	0.1 cc.	0.1 cc.

Second row same as above, omitting antigen and using 0.2 cc. buffered saline solution throughout.

Place rack in refrigerator (about 8° C.) for one hour, then in water bath (37½° C.) for ½ hour; add 0.1 cc. haemolytic system (equal quantities of 1:20 sheep cells and about 2½ units of haemolysin), incubate 30 minutes longer in water bath and take readings.

As this is not a very sensitive antigen, the dilution of complement showing almost complete haemolysis in titration tube containing antigen, and complete haemolysis in the saline control tube is considered one unit, and in the final test 2, 2½ and 3 units are used. Example for test:

4 tubes for each specimen:	*1*	*2*	*3*	*4*
Serum (1:10)	0.1 cc.	0.1 cc.	0.1 cc.	0.2 cc.
Antigen dilution	0.1 cc.	0.1 cc.	0.1 cc.	omit
Complement	0.1 cc. (2 units)	0.1 cc. (2½ units)	0.1 cc. (3 units)	0.1 cc. (2 units)

Include one rack containing 0.1 and also 0.2 cc. antigen controls (without serum) and several negative and positive serum controls from the previous day's test.

After addition of complement, the racks are placed in refrigerator (about 8° C.) overnight. Next morning, 0.1 cc. haemolytic system (made up just before needed) is added throughout, to the control rack first and then to the remaining racks, one or two at a time. Each rack is timed as it is placed in the water bath at 37.5° C. Readings are made when the sera in control rack are haemolysed to approximately the same degree as in the previous day's test, and when antigen controls with 0.1 cc. and 0.2 cc. show CH and ACH plus, respectively. Time required is usually twenty to thirty minutes.

Racks are, of course, thoroughly shaken after addition of each reagent.

The method of reporting readings has been as follows:

Original Terminology	*Later Terminology*
4440 (3 units of comp.)	4 plus plus
4430 (2½ " " ")	4 plus
4300 (2 " " ")	3 plus
3100 (1½ " " ")	2 plus
2000 (1 " " ")	1 plus
Neg. to 1000	negative

That Caulfeild considered these tests simply as an aid in diagnosis, is apparent in the following quotation from article[1] previously mentioned: "Serological tests afford no clinical diagnosis but suggestions which should be eliminated or confirmed by other clinical methods."

These tests were first carried out under the supervision of Doctors A. W. H. Caulfeild,* and W. Ray Hodge,* of the Research Division of the Connaught Antitoxin Laboratories, and later under the supervision of Dr. A. C. Norwich, as Director of Laboratories, Christie Street Hospital, Department of Veterans Affairs. Assistant serologists at various times were Mina Macmillan, Florence La-Rush,* Merle Bassingthwaight, and Dorothy Kitchen.

*Deceased.

REFERENCE

1 Caulfeild, A. H. W., et al.: "The Tuberculo-Complement-Fixation and Inhibitive Tests," *Am. Rev. Tuberc.*, 11:6, (August) 1925.

Laryngo-Tracheo-Bronchial Anesthesia for Bronchoscopy and Bronchography with Pontocaine

A. ALBERT CARABELLI, M.D., F.A.C.P., F.C.C.P.*
Trenton, New Jersey

Review of the literature shows a considerable variety of techniques in laryngo-tracheo-bronchial anesthesia for the procedures of bronchoscopy and bronchography. The variation is noticed in both the procedures themselves as well as in the type and quantity of the topical anesthetic. The adjuvant medication also shows a considerable difference in the types of the drugs used. The most common surface anesthetics appear to be cocaine and pontocaine. Others in use are nupercaine (Rudman[17]), larocaine (Benedict[1]), butyn (Sante[18]), and methycaine (Rudman[17]). Larocaine appeared to be a promising drug which the author and others (Jackson and Jackson,[12] Moorhead,[14] and Benedict[1]) have used with good results. Unfortunately the manufacturer (Hoffman La Roche) no longer produces this drug. In a survey conducted by Moorhead[14] it was noted that 50 per cent of his correspondents used cocaine as an anesthetic. Different authors have employed these drugs alone or in combination with each other. The quantities used vary tremendously and at times it was difficult to determine the actual amount administered as the article merely gave the percentage of the solution without specifying the total amount. In many instances an undeterminable amount was used in sprays, swabs, or tampons, making a quantative appraisal impossible. For these reasons comparative tabulation of the amounts of the drugs introduced by the various authors could not be made in all cases. Even the articles tabulated had to have provision made for the unmeasured loss in swabs, etc.

In this study it was decided to employ pontocaine since it was felt that more and more use was being made of this drug, and that it was considered more free from the toxic reactions which occurred with cocaine (Benedict[1] and McReynolds[13]).

With respect to the adjuvant drugs, each author appears to have his own favorite. This is an understandable situation since long-continued use of any one particular drug soon makes one

*Chief of Thoracic Medicine, St. Francis Hospital, Trenton, New Jersey. Associate in Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

familiar with its potency in various patients as well as with its idiosyncrasies. The drugs commonly used were morphine, ether alone or in combination with atropine, dilaudid, scopalamine, codeine, nembutal, sodium pentobarbital, and demerol. It was not surprising to find that the barbiturates were almost universally used in conjunction with pontocaine because of their neutralizing action in preventing the toxic symptoms occasionally seen after the administration of pontocaine. Adrenalin hydrochloride (1/1000) was also employed by most authors in various amounts added to the pontocaine solution to reduce too rapid absorption of the anesthetic agent.

Pontocaine as presently used is not in itself free from its measure of toxicity (Criciani and Nogeura,[5] Thomas and Fenton[22]) and its quota of deaths (Derbes and Engelhardt,[7] Richards,[16] Schindler,[19] Schoen,[20] Hansen and Stealy[8]). Reported and unreported cases of sudden death have been fairly well attributed to the drug alone. Critical reviews of the deaths indicate that in almost all cases excessive quantities of the drug have been given. The advent of the barbiturates supposedly controlled the toxic reactions; however, deaths were still observed in spite of the apparent safety which the barbiturates conferred. If the recommendations of the manufacturer on the maximum safe dosage of the pontocaine to be used for the procedures of bronchoscopy and bronchography is correct, it would appear that practically all workers who stipulate the quantity of pontocaine are employing excessive and unsafe dosages.

Tuohy[24] stressed that the important point to remember in the use of local anesthetics is that they must be used in small amounts. There was no question that the main difficulty in the successful use of pontocaine was one of quantity. The barbiturates though helping considerably were not the entire answer in preventing deaths. The manufacturer, in the pamphlet that accompanies the stock bottle, plainly stipulates that the maximum *safe* dose for intra-tracheal instillation should not exceed one cubic centimeter (1 cc.) of the 2 per cent solution or its diluted equivalent. The total for this safe dose is twenty milligrams (20.00 mgms.). Another admonition which the pamphlet stresses is that the patient, to prevent entrance of the drug into the lungs, should not inhale too deeply. Any bronchoscopist or bronchographer can readily see the impossibility of attempting to follow these tenets and yet be able to perform either one of these procedures properly under local anesthesia. The amount of the solution recommended was in most cases definitely too small for proper manipulation with spray and cannula; and no patient could be kept from unconsciously taking deep breaths while being anesthetized. As

a matter of fact in most cases the patient is encouraged to take deep breaths to spread the solution throughout the tracheobronchial tree. A self-consciousness on solution strengths was apparently present in the minds of almost all users of pontocaine since their articles revealed the use of several percentages of the solution below 2 per cent in order to increase the bulk of the solution for proper manipulation.

Review of the literature confirmed the anomalies between the recommendations of the manufacturer and the practical use of the solution. It was discovered that almost no worker was able to employ the recommended dose, but always exceeded it. The amounts actually used (See Table I) varied from two and one half cubic centimeters (2.5 cc.) (Titche[23]) for bronchoscopy to fifteen cubic centimeters (15 cc.) (Poppe[15]) of the 2 per cent solution for bronchography! Many authors, especially bronchoscopists could not be included in the tabulation because their articles were too vague on the actual amount of the solution used, merely mentioning the percentage of solution.

In view of the above concepts and impracticalities; and on the basis that the manufacturer probably had ample experimental work upon which to base the maximum safe dosage, it was decided to study the generally used strengths in the hope of finding an

TABLE I

Review of the Literature on Quantaties of Pontocaine Used for Bronchoscopy and Bronchography

	PONTOCAINE			
Procedure	Mgms.	Equivalent of 2 Per cent Sol. in cc.	Working Dilutions Per cent	Author
Bronchoscopy	50	2.5	2-0.5	Titche[23]
Bronchoscopy	50*	2.5*	2-0.5	Heublein[10]
Bronchography	20*	1*	1	Sommerfield[21]
Bronchography	40*	2*	2	Boyer[3]
Bronchography	50-100	2.5-5	2, 0.25, 0.15, 1/1000	Castellanos[4]
Bronchography	60	3	2	Harwood[9]
Bronchography	65	3.25	0.5	Hughes[11]
Bronchography	120, 140, 160*	6, 7, 8*	2	Dell[6]
Bronchography	300	15	1	Poppe[15]

*Indicates undetermined amounts used in addition to the above quantities in sprays, swabs, or tampons.

effective low strength with sufficient volume for properly anesthetizing the tracheo-bronchial tree. It was felt that pontocaine was potent enough in low dilutions to be used for these purposes. The lowest uniform strength that would be effective could not be learned from the literature since most authors employed a combination of strengths beginning with the 2 per cent solution and decreasing the strength down to 1 and 0.5 per cent or even lower. The higher strengths were usually employed in the preliminary anesthetization of the mouth and pharynx, apparently on the theory that these structures are more tolerant to the stronger solution (Schindler[19]) than the larynx, trachea, and bronchi. One article (Castellanos, Pereiras, and Montero[4]) mention the use of two to four cubic centimeters (2-4 cc.) of the 2 per cent solution for the mouth and pharynx and 0.25 per cent or even 0.15 per cent solution for the trachea and bronchi. On occasions these same authors have used a 1/1000 solution.

It was at once apparent when the literature was studied that the problem with respect to the solution was one of sufficient bulk to permit instillation and spread into the tracheo-bronchial tree. At the same time this solution had to be of such strength that it would be nontoxic, but still give an effective, sustained anesthesia to permit a leisurely performed bronchoscopy or bronchography; and yet meet the manufacturer's limitation of total dosage. No such one-strength solution was being used in the literature. Trial and error evolved a solution of 0.25 per cent strength which was found effective for surface anesthesia in bronchoscopy and bronchography. This solution was made by placing one cubic centimeter (1 cc.) of 2 per cent pontocaine into a ten cubic centimeter (10 cc.) glass cylinder, adding eight minims of adrenalin hydrochloride (1/1000) and diluting to eight cubic centimeters (8 cc.) with sterile physiological salt solution. This solution was considered ideal inasmuch as it had already been tested for sufficient surface anesthesia and had what appeared to be the proper bulk to manipulate. It also had the vasoconstrictor action which most workers desired because of the adrenalin content.

Having standardized the one-strength solution, it was decided to standardize the adjuvant medication for purposes of control. Morphine in combination with atropine in full doses was used simply because the author was more familiar with its action than other drugs and probably the same could be said with other authors since most of them use this combination. No barbiturates were added in this study. It was noticed with this combination and with the use of the 0.25 per cent solution that excellent patient control and surface anesthesia were obtained. However,

it was also noticed that more than eight cubic centimeters (8 cc.), which was the total volume that could not be exceeded, was administered thus defeating the theoretical intended use of only twenty milligrams of pontocaine (1 cc. of the 2 per cent or 8 cc. of the 0.25 per cent solution). It was also noted that the standard atomizer as well as the laryngeal mirror and cannula technique left much to be desired when a critical study of their use was made. For quantative conservation of solution this procedure interposed many difficulties and uncertainties which resulted in a waste of about 50 to 60 per cent of the solution most of which was swallowed or expectorated. The ordinary methods of laryngo-tracheo-bronchial anesthesia have not been improved upon for many years and it was felt that something could be done to effect "economy of solution" by a better armamentarium.

One improvement, of course, was the elimination of the third hand about the mouth orifice. In the usual method the operator first holds the atomizer in both hands (some are skilled enough to use the standard atomizer as a "one-hand" type) while the patient or an assistant retracts the tongue for the spraying procedure. It was felt that the use of a "one-hand" atomizer could dispense with the third hand at this stage. A handle was accord-

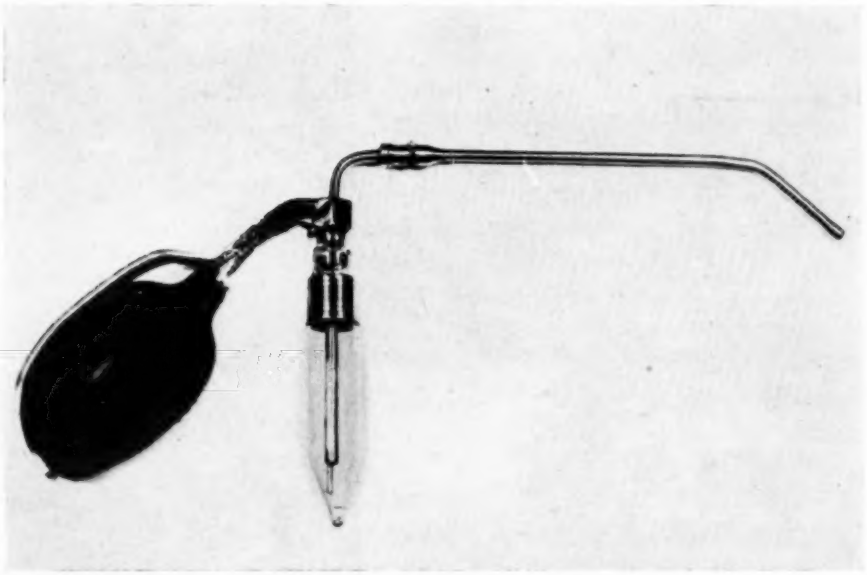


FIGURE 1: This micro-atomizer was developed from the stock Clerf atomizer in frequent use by bronchoscopists. The original cannula was shortened and given the oro-pharyngeal curve. The atomizer was made with a handle to make it of the "one hand" type with a double valve in its bulb which gives better, sustained compression as well as easier hand pressure than the one valve type. The reservoir is of boilable glass with a capacity of about eight cubic centimeters (8 cc.) and is the same as that used on the Clerf atomizer so that the residual anesthetic can be transferred to the Clerf atomizer by simply exchanging reservoirs.

ingly fitted to a standard No. 15 De Vilbiss atomizer and this arrangement found fairly satisfactory except that the standard atomizer had too coarse a spray and too capacious a reservoir to properly effect "economy of solution." A special atomizer was then designed by the author which met the specifications of a small reservoir and a fine spray (Fig. 1).

The next step studied was the use of the separate laryngeal mirror and cannula. Here the greatest waste was noted. In spite of the fact that this method had been used by the author for many years, its short-comings were not noticed until the present critical study. The operator had no choice but to have either the patient or an assistant hold the tongue. When the patient held the tongue, its dorsum would eventually be humped up and almost completely block the line of vision. The operator had to work more or less blindly, most of the time instilling the solution with the hope that it would drop upon the cords and into the trachea. Even with the most cooperative of patients, it was noticed that a full view of the cords was only rarely had. A goodly portion of the solution trickled down the pyriform sinuses and was swallowed. When an assistant held the tongue, usually too much traction was made, resulting in pain or excessive salivation and gagging. If too little traction was made, there was humping of the dorsum again with poor visibility of the cords. It is true that some operators are skilled in effectively using this procedure; but when critical quantities of solution are being considered, it was felt that a more accurate localization of the structures involved as well as the direction of flow of the anesthetic were needed so that only those structures intended were anesthetized and the solution not wasted into the esophagus.

To facilitate this second step a simple mirror-cannula was devised[3a] which permits the operator to hold the tongue himself and to make the necessary traction coordinate with the instillation of the solution. Complete visibility of the posterior portion of the epiglottis as well as of the vocal cords is had at all times with this cannula. Solutions can be accurately instilled only where intended without wastage.

Techniques for Bronchoscopy and Bronchography, Using the Micro-atomizer and Mirror-cannula.

1) *Basic "one-strength" solution (0.25 per cent Pontocaine).* This solution is simply made by adding one cubic centimeter (1 cc.) of 2 per cent stock solution of pontocaine to a ten cubic centimeter (10 cc.) glass cylinder. Eight minims of adrenalin hydrochloride (1/1000) are then added and the solution brought

up to a total volume of eight cubic centimeters with sterile physiological salt solution.

2) *Bronchography.* The basic solution alone without the adjuvant medication is used for this procedure. The mirror cannula is used only for anesthetization and not for the introduction of the catheter. Spraying of the mouth and pharynx is done at ten minute intervals using the solution in the micro-atomizer sparingly. In about 20 to 30 minutes it is possible to instill several cubic centimeters of the basic solution upon the cords and into the trachea with the mirror-cannula. This is followed by the introduction of a rubber catheter (No. 14 or 16 F) on a Thompson wire introducer. Occasionally it may be necessary to introduce more of the solution through the rubber catheter if too strong a cough reflex is caused by the catheter. With this technique it is possible to obtain good bronchograms with eight cubic centimeters and frequently less of the solution.

3) *Bronchoscopy.* The patient is given the morphine and atropine in full physiological dose. The dosage may be increased or decreased "secundum artem" depending upon the type and size of the patient. Thirty minutes later the mouth and pharynx are sprayed with the micro-atomizer which contains about three cubic centimeters (3 cc.) of the basic solution. Care is taken to fully retract the tongue and to have the patient inhale with each spraying. It was not found necessary to spray too heavily for effective anesthesia. Two or three squeezes of the bulb usually suffice. Ten minutes later a second spraying is done which is repeated again in ten minutes. In about five minutes it will be discovered that the patient experiences the sensation of numbness and inability to swallow which indicates proper anesthesia. At this point he is placed on an ear, nose, and throat chair, the tongue retracted, and one cubic centimeter (1 cc.) of the solution instilled upon the vocal cords and into the trachea. The solution which is used for this procedure is the balance of the original eight cubic centimeters (8 cc.) that had been prepared. It is placed in a medicine glass and taken up into the syringe attached to the mirror-cannula in one cubic centimeter or more portions as needed. It will be noticed that as soon as the solution strikes the tracheal mucosa a cough is elicited. The introduction of the solution is made gently and deliberately, drop by drop. Following the instillation the patient is asked to cough with his mouth closed. This permits the solution to be spread evenly throughout the tracheo-bronchial tree. Five minutes later a second instillation of about one cubic centimeter (1 cc.) is made in the same manner. At this time the cough is considerably obtunded with a marked change in its timbre and indicates that the patient is

ready for bronchoscopy. If the cough is still high-pitched, a third instillation may be indicated. The procedure must not be hurried; nor too great quantities of solution instilled. One must refrain from "pouring in" the solution as the quantities recommended will be found of sufficient strength for proper surface anesthesia. The patient is then placed on the bronchoscopic table and given the sermon on relaxation as advocated by Jackson and Jackson.[12] This, as well as a darkened room, quiet, and a sympathetic attitude are of the utmost importance in successful bronchoscopy. The author makes it a rule to describe the procedure to the patient, but only when he is on the table.

Prior to introducing the bronchoscope the remaining solution in the medicine glass is transferred to the reservoir of the micro-atomizer which may still have some of the solution which was used for spraying. This reservoir is then attached to the Clerf atomizer for endo-bronchial spraying. It will be noted that the reservoirs of the micro-atomizer are the same as those used in the Clerf atomizer and therefore interchangeable. The bronchoscope is introduced in the usual manner and when it reaches the carina, the right and left main stem bronchi are anesthetized by spraying very sparingly with the Clerf atomizer which now contains the residium of the original basic solution. On occasions it will be found that spraying of the bronchi will not be necessary. After several minutes of waiting, it will be possible to procede with the bronchoscopy satisfactorily. Occasionally a patient is encountered who will cough when the bronchoscope is introduced far down distending the lumen with its bulk. When this contingency occurs the bronchoscope is slightly withdrawn relieving the pressure and the area gently sprayed with the Clerf atomizer. This procedure apparently satisfactorily controls the cough reflex.

Following the completion of the bronchoscopy the residual anesthetic that is left in the Clerf atomizer is placed in the ten cubic centimeter glass cylinder and the total quantity used for the entire procedure of oro-pharyngo-laryngo-tracheo-bronchial anesthesia determined by subtracting what is left from the original volume of eight cubic centimeters (8 cc.). It is advocated that this be done in every case and recorded as it enables the operator to become "solution conscious" and makes him strive to conserve at all stages.

In the series of bronchoscopies reported oxygen insufflation through the side arm of the bronchoscope was used at the rate of six liters per minute as it was felt that the entire procedure was facilitated and relieved the patient of the sense of suffocation which is frequently noticed during bronchoscopy without oxygen.

4) *Simultaneous Bronchoscopy and Bronchography.* The author has been recently performing both bronchoscopy and bronchography at the same sitting with the same amount of anesthesia as is used for bronchoscopy. The technique will be reported in a later communication, but is mentioned here inasmuch as it has been used in many of the patients reported in this series and since it further shows that pontocaine even in dilute solution is capable of prolonged and sustained surface anesthesia.

Results. A total of 167 consecutive, unselected, bronchoscopies in adults were performed with the technique and innovations of instruments mentioned above. With the exception of eight cases all were ambulant patients. The eight were hospitalized for other reasons than their pulmonary manifestations. The series was considerably varied and included the following types of patients: Broncho - sinusitides, asthmatics, compensated cardiac diseases, hypertensives, stabilized coronary disease, lung abscesses, bronchiectases, pulmonary neoplasms, Hodgkin's disease, empyemata, atelectases, broncho-pulmonary suppurations, pulmonary tuberculosis, bronchial ulcerations, bronchostenoses, advanced age, and one case of severe cervico-dorsal kypho-scoliosis associated with bronchiectasis. It will be seen from the above list that the series gave the opportunity to study the technique in the usual collection of cases that may come to bronchoscopy. Many cases proved to have negative findings in spite of the fact that they presented pulmonary symptomatology of what could have been either endobronchial or endotracheal lesions; so, it may be said, that the procedure was also used in "normal" cases.

The oldest patient was 70 and the youngest 19 years of age. The average age was 39.3 years and the average weight 138.3 pounds.

To judge the adequacy of the anesthesia from the point of view of the patient, notes were kept on the cooperation of the patient as well as of the amount of coughing during the procedure of bronchoscopy. With the exception of eight (8) cases, the patients behaved well; coughed very little; and the bronchoscopy was carried out leisurely and deliberately. In these eight cases, however, there was considerable cough which necessitated additional surface anesthesia. They are discussed below. A "head-holder" was not used in any case and the entire procedure was carried out by the operator with one instrument nurse. All were strictly ambulant except the cases previously mentioned who were already in the hospital for other reasons. No ambulant case required hospitalization after bronchoscopy for any reason whatsoever.

Excessive secretions in the oro-pharynx were noted in only four of the patients. These required aspiration before bronchoscopy could be performed. One case salivated so profusely that the secre-

TABLE II

Drug Dosage in 167 Consecutive Bronchoscopies in Adults

	PONTOCAINE				
Cases	Mgms.	Equivalent of 2 Per cent Sol. in cc.	Working Solution cc. of 0.25 Per cent	Morph. Sulf. Mgms.	Atrop. Sulf. Mgms.
1	40.00	2.000	16.00	22.50	0.60
1	40.00	2.000	16.00	7.50	0.20
2	30.00	1.500	12.00	15.00	0.40
2	30.00	1.500	12.00	7.50	0.20
2	25.00	1.250	10.00	15.00	0.40
3	20.00	1.000	8.00	22.50	0.60
61	20.00	1.000	8.00	15.00	0.40
8	20.00	1.000	8.00	7.50	0.20
2	18.75	0.937	7.50	15.00	0.40
8	17.50	0.875	7.00	15.00	0.40
1	17.00	0.850	6.80	15.00	0.40
1	17.00	0.850	6.80	11.25	0.30
38	15.00	0.750	6.00	15.00	0.40
1	15.00	0.750	6.00	11.25	0.30
1	15.00	0.750	6.00	7.50	0.20
1	14.50	0.725	5.80	15.00	0.40
10	12.50	0.625	5.00	15.00	0.40
1	12.50	0.625	5.00	22.50	0.60
2	12.50	0.625	5.00	11.25	0.30
1	12.50	0.625	5.00	7.50	0.20
1	12.00	0.600	4.80	15.00	0.40
2	11.87	0.594	4.75	15.00	0.40
3	11.25	0.563	4.50	15.00	0.40
2	11.25	0.563	4.50	11.25	0.30
1	11.00	0.550	4.40	15.00	0.40
1	10.05	0.525	4.20	15.00	0.40
3	10.00	0.500	4.00	15.00	0.40
1	10.00	0.500	4.00	11.25	0.30
1	9.37	0.468	3.75	11.25	0.30
1	8.75	0.438	3.50	15.00	0.40
1	8.75	0.438	3.50	11.25	0.30
1	7.50	0.375	3.00	11.25	0.30
1	6.25	0.312	2.50	11.25	0.30
1	5.00	0.250	2.00	11.25	0.30
Tot. 167	2890.66	144.508	1156.05	2400.00	64.00
Average	17.37	0.865	6.92	14.43	0.383
"Normal"	20.00	1.000	8.00	15.00	0.400

tions ran into the lung alongside the bronchoscope and required continuous aspiration.

Table II gives the actual dosage of the pontocaine in milligrams and equivalents in cubic centimeters of a 2 per cent solution as well as of the 0.25 per cent solution which was actually used. The comparison with the 2 per cent solution is made because a better concept is had of the small amounts of pontocaine used. The table also gives the milligrams of morphine and atropine. It will be noted that only eight (8) cases required dosages higher than those recommended by the manufacturer, but still less than any reported in the literature for bronchoscopy. Three of these cases had only 7.50 milligrams of morphine and it is felt that the total quantity of pontocaine could have been reduced had full doses of morphine been employed. One case was a chronic alcoholic of such physical mien that the full dose of 40.00 mgms. of pontocaine and 22.5 mgms. of morphine were entirely needed. He was the most difficult of the series. One with pulmonary abscess had the entire tracheo-bronchial tree coated with a tenacious, muco-purulent secretion which prevented the anesthetic from reaching the mucosa. It was noted throughout the series that cases of pulmonary abscess and advanced bronchiectasis were difficult to anesthetize for the same reason. Three cases were not exceptional in any manner and the excess dosage could not be based on any particular reason except that they were done early in the series before the technique was well mastered. These eight cases of "over-dosage" are analyzed in Table III.

The actual chronological protocol of cases roughly parallels the decrease in dosage shown in the table. The gradual decrease was

TABLE III

Analysis of Cases of "Over-Dosage" (8 Cases)

Age	Weight lbs.	Sex	Pontocaine Mgms.	Morph. Sulf. Mgms.	Atrop. Sulf. Mgms.	Remarks
46	171	M	40	22.5	0.6	Chronic alcoholic
65	165	F	40	7.5	0.2	Carc. LUL with bronchostenosis, severe
46	121	F	30	15.0	0.4	Normal findings
54	136	F	30	15.0	0.4	Abscess RML
48	155	F	30	7.5	0.2	Normal findings
38	129	M	30	7.5	0.2	Abscess LUL
34	180	M	25	15.00	0.4	Normal findings
29	180	M	25	15.0	0.4	Normal findings

possible as the operator became more skilled with the technique. It will be noted that several large groups (61 and 38 cases) had uniform doses. This standardization occurred when the author thought he had reached two minimum levels below which he could not go without losing the effect of the anesthetic. Subsequent cases proved, however, that a personal variable was present with each patient and that each one had his own level of susceptibility to the action of pontocaine. The operator soon got the "feel" of the anesthetic action and instilled only sufficient quantities. It will be further noted that 72 cases were done with the equivalent of one cubic centimeter (1 cc.) of the 2 per cent solution (20.00 mgms.) and that 87 cases with the equivalent of less than one cubic centimeter of the 2 per cent solution (less than 20.00 mgms.).

The average dose for the entire series was the equivalent of 0.865 cc. of the 2 per cent solution or 17.37 milligrams of pontocaine. The average dose of morphine was 14.43 milligrams and that of the atropine 0.383 milligrams. All these dosages are well within the safe limits of posological tables and, with respect to the pontocaine, below the maximum recommended dose of the manufacturer.

Complications and Sequelae. In spite of the fact that no barbiturates were used in any case of the series, no case presented any symptomatology which could be construed as a reaction to pontocaine. The eight cases of "over-dosage" were watched closely and showed no immediate or delayed ill-effects from this drug. In the series were included six cases of severe asthma who had been personally seen in asthmatic crises on various occasions leaving no doubt as to the diagnosis with respect to their allergy. These patients were also closely watched for any toxic manifestations or precipitation of asthmatic crises inasmuch as reactions to this drug in asthmatics have occurred with sufficient frequency that Jackson and Reynolds as quoted by Benedict[2] have stated that pontocaine is contra-indicated in asthmatics. Criciani and Nogeura[5] have reported the production of asthmatic crises by the intratracheal instillation of pontocaine. The results in the six cases constitutes too small a series to draw any definite conclusions when compared with the more complete studies by the authors just mentioned; and the absence of complications in these asthmatics might have been purely a fortunate coincidence.

SUMMARY

1) Review of the literature shows that all authors committing themselves on the actual quantity of pontocaine used for bronchoscopy or bronchography are using far more of the drug than

is recommended by the manufacturer. In one case as much as fifteen times the recommended dose was used for bronchography.

2) Unnecessarily large amounts of pontocaine are used for these procedures because of the inadequacies inherent in present techniques and instrumentarium.

3) A "one-hand" micro-atomizer and mirror-cannula which permit use of small doses of pontocaine are described.

4) A technique which makes possible bronchoscopy and bronchography with the use of 20.00 mgms. (1 cc. of 2 per cent solution) or less of pontocaine as a 0.25 per cent solution with only morphine and atropine in full doses as adjuvent sedation is described.

5) An unselected, consecutive, series of 167 bronchoscopies in adults performed with these techniques using an average of 17.37 mgms. of pontocaine (0.865 cc. of 2 per cent solution) with no complications attributable to pontocaine is reported.

6) This entire series was performed without the use of any barbiturate to counteract the reactions to pontocaine.

7) Pontocaine in 0.25 per cent solution is a safe, effective, and long-lasting surface anesthetic suitable for the procedures of bronchoscopy and bronchography.

RESUMEN

1) La revista de la literatura revela que todos los autores que se han declarado acerca de la verdadera cantidad de pontocaína que usan para la broncoscopia o la broncografía están usando una cantidad de la droga mucho más grande de la que recomienda el fabricante. En un caso se usó para la broncografía una cantidad quince veces más grande que la dosis recomendada.

2) Se emplean cantidades supérfluas de pontocaína en estos procedimientos debido a las imperfecciones inherentes a las técnicas e instrumentos que se usan actualmente.

3) Se describe un micro-pulverizador y espejo-cánula usados con una sola mano, que permiten el empleo de dosis pequeñas de pontocaína.

4) Se describe una técnica que permite la ejecución de la broncoscopia y la broncografía, con 20.00 mg. (1 cc. de una solución al 2 por ciento), o menos, de pontocaína en una solución al 0.25 por ciento, con dosis completas de morfina y atropina como sedantes auxiliares.

5) Se informa sobre una serie consecutiva, no seleccionada, de 167 broncoscopias en adultos llevadas a cabo mediante estas técnicas, usando un promedio de 17.37 mg. de pontocaína (0.865 cc. de una solución al 2 por ciento), sin ninguna complicación imputable a la pontocaína.

6) Se llevó a cabo esta entera serie sin usar ningún barbiturato para neutralizar las reacciones a la pontocaína.

7) La pontocaína en solución al 0.25 por ciento es un anestésico de superficie salvo, eficaz y de acción prolongada, adaptable a los procedimientos de la broncoscopia y la broncografía.

All the instruments mentioned in this paper including the mirror-cannula and the micro-atomizer are available from the George P. Pilling & Sons Company, 3451 Walnut Street, Philadelphia, Pennsylvania, to whom the author has given the specifications for the manufacture of both these instruments.

REFERENCES

1 Benedict, Edward B.: "Medical Progress: Endoscopy," *New England J. Med.*, 228:253, 1943.
2 Benedict, Edward B.: "Endoscopy," *New England J. Med.*, 226:449, 1942.
3 Boyer, L. Bryce: "Bronchography in Tuberculosis," *Am. Rev. Tuberc.*, 54:111, 1946.
3a Carabelli, A. Albert: "A New Mirror-Cannula for Laryngo-Tracheo-Bronchial Anesthesia, Medication or Instillation of Opaque Oils," *Dis. of Chest*, 15:107, 1949.
4 Castellanos, A., Pereiras, R. and Montero, R.: "Tecnica Bronchographía en el Niño," *Bol. Soc. Cubana de Pediat.*, 12:594, 1940.
5 Criciani, J. A. and Nogeura, O.: "Experimental Production of Asthma Crises by Intratracheal Instillation of Tetracaine," *La Prensa Med., Argentina*, 28:1791, 1941.
6 Dell, J. M. Jr.: "Bronchography," *Southern M. J.*, 40:543, 1947.
7 Derbes, Vincent J. and Engelhardt, Hugo T.: "Deaths Following the Use of Local Anesthetics in Transcricoid Therapy," *J. Lab. and Clin. Med.*, 29:478, 1944.
8 Hansen, F. M. and Stealy, Clair L.: "Sudden Death Following the Use of Pontocaine as a Gargle for Gastroscopic Examination," *Rev. of Gastro-enterology*, 10:212, 1943.
9 Harwood, H. B.: "Bronchiectasis," *Med. J. of Australia*, 1:65, 1945.
10 Heublein, Gilbert W. and Gilfillan, Clarence D. N.: "A Practical Technique for Visualization of the Bronchial Tree," *Radiology*, 48:37, 1947.
11 Hughes, John D.: "The Development and Early Diagnosis of Bronchiectasis," *Jour. Tennessee Med. Assoc.*, 38:355, 1945.
12 Jackson, Chevalier and Jackson Chevalier L.: "Bronchoscopy, Esophagoscopy, and Gastroscopy," *W. B. Saunders Co.*, Philadelphia, 1934, pp. 76-82.
13 McReynolds, George S. Jr. and Shelton, Fred W.: "Bronchography as a Diagnostic Aid in Chest Diseases," *Ann. Otology, Rhinology and Laryngology*, 44:114, 1945.
14 Moorhead, Robert L.: "Symposium on Peroral Endoscopy," *Laryngoscope*, 49:1162, 1939.
15 Poppe, J. Karl: "A Simple and Practical Method of Obtaining Complete Bronchograms," *Am. Rev. Tuberc.*, 54:104, 1946.
16 Richards, Robert: "A Note on the Causation of Sudden Death," *British Med. J.*, 2:51, 1947.
17 Rudman, L. Ellis: "Bronchial Catheterization," *Am. Rev. Tuberc.*, 39: 329, 1939.
18 Sante, L. R.: "The Chest," *Paul B. Hoeber, Inc.*, 1936, pp. 19-25.
19 Schindler, Rudolf: "Results of the Questionnaire on Fatalities in Gastroscopy," *Am. J. Digest Dis.*, 7:293, 1940.
20 Schoen, Ferdinand: "Fatal Medical Reactions to Pontocaine," *Wien Klin. Wehnschr.*, 52:505, 1939.
21 Sommerfield, Ralph B.: "An Anesthetist's Interest in Lipiodo-Bronchography," *Anesthesiology*, 3:61, 1942.
22 Thomas, J. W. and Fenton, M. M.: "Fatalities and Constitutional Reactions Following the Use of Pontocaine," *Jour. Allergy*, 14:145, 1942.
23 Titche, Leon L.: "Anesthesia in Tracheobronchial Procedures," *Dis. of Chest*, 13:452, 1947.
24 Tuohy, Edward B.: "Practical Concepts in Anesthesia," *Ohio State M. J.*, 43:148, 1947.

Intratracheal Atomization in the Treatment of Infectious Diseases of the Respiratory System

Preliminary Report

PEDRO L. FARIÑAS, M.D., F.C.C.P.,
O. SUAREZ de BUSTAMANTE, M.D., F.C.C.P.,
LUIS M. LOTT, M.D., F.A.P.H. and RENE REVUELTA, M.D.
Havana, Cuba

The treatment of infectious diseases of the respiratory tract with aerosols has become quite popular during the last few years, due in particular to the use of antibiotics. At present, nebulizers are used for this procedure in which the thick particles are condensed in the apparatus allowing only the outflow of very fine and small particles, less than two micra in diameter.

The common sprayers cause an outflow of droplets much thicker and we have demonstrated in our works on Mucosography of the Respiratory System (Radiology, July 1942) that these droplets reach by gravity and pulmonary aspiration the terminal bronchi and the pulmonary alveoli.

Harold A. Abramson of the Staff of the Commanding General Technical Division, Chemical Warfare Service, in his work on Aerosol Therapy of the Lung and Bronchi with Special reference to Penicillin and Hydrogen Peroxide (New England Medical Center, VIII, 1946), recommends the use of our technique of atomization in the general treatment of the diseases of the respiratory system where great amounts of liquids should be used.

We began our studies in the Department of Tuberculosis of the Faculty of Medicine of the University of Havana (Instituto de Vías Respiratorias, Servicio del Profesor Doctor A. Antonetti). We selected a group of patients who presented different pulmonary suppurations such as bronchiectasis, abscess of the lungs, gangrene of the lungs, etc. The first part of our investigation was directed to prove under what conditions could this method be applied. The anesthesia to be used was considered, the volume and concentration of the solution used, and its tolerance by the bronchial tract.

Tests were performed with penicillin, streptomycin, hydrogen peroxide and sulfa drugs. Finally we decided to use penicillin in the first series of applications, bearing in mind its antibiotic action and its known tolerance.

Direct examination was made of the patients sputum from the

bacteriological point of view. Cultures were carried out routinely in all the cases. Several determinations in series were performed to demonstrate the levels or concentrations of the antibiotics in the blood. Other determinations were made for the purpose of studying the conditions of absorption, retention or elimination of antibiotics in the sputum. Comparative studies with other methods of therapy by inhalation were made.

Technique

The technique of intratracheal atomization is not a difficult one. We take a long sprayer that gives a very fine atomization, the end may be placed easily in the larynx, behind the epiglottis (Fig. 1) or in the trachea under the vocal cords. The apparatus we designed is very satisfactory and we are pleased with the results obtained.

We start our procedure by anesthetizing the pharynx, larynx and the trachea by spraying a solution of ½ per cent pantocaine. During the atomization of the pantocaine we have the patient lean towards the side we are going to treat and we have him inhale strongly in order to anesthetize the trachea and the bron-

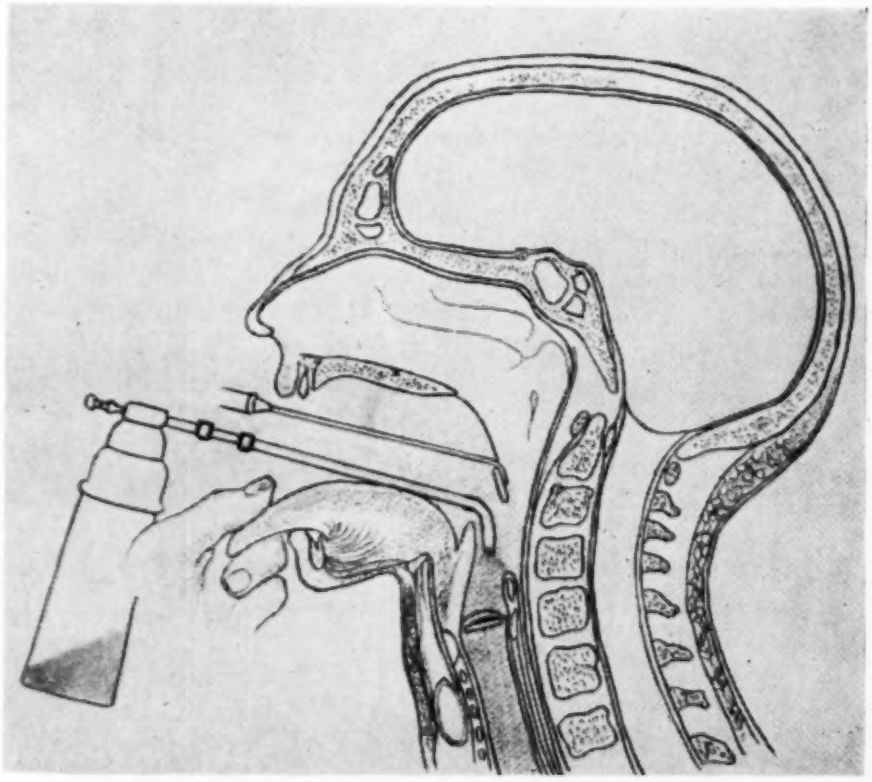


FIGURE 1: The atomizer in the larynx above the vocal cords.

chial tract on that side. After waiting a few minutes so that the anesthesia is well established, we place our sprayer in the trachea and then commence to spray with the solution we have adopted for this technique. Before the sprayer is placed in the trachea, its container is connected to a rubber tube with an air compressor allowing a pressure of six or seven pounds. The patient must be seated in a straight position with the head straight up and the body completely bent towards the side we are going to treat, and bent to the front or to the back according to the pulmonary segment which is the object of the treatment. Right after the atomization the patient is placed in a special position corresponding to the pulmonary segments where the lesion is located and must remain in this position as long as possible trying not to cough. Trendelemburg's position should be always used for the upper lobe. The quantity of the spray solution varies according to the kind of diseases and the substance used, 20 cc. of an aqueous solution may be sprayed in one or two minutes.

Laboratory Investigations:

For the exact bacteriological control of the sputum we have used 5 per cent blood-agar as culture medium. The determination of the antibiotic action was done following the technique of the Oxford investigators: in Petri dishes with solid agar medium, we add staphylococcus aureus (strains received from Washington) culture diluted to 1/10. After keeping it 24 hours in refrigerator, it is placed on the surface of the agar. The rings are filled with the blood, sputum or other secretions to be tested for antibiotic properties. The Petri dishes are refrigerated for 24 hours, after this period of time all the liquid in the inside of the rings has disappeared by difussion through the agar. We observed circular zones of inhibition of the culture in the dish where no bacteria develops. With a millimeter crystal ruler we determine the diameter of the zone of inhibition. This diameter demonstrates the extent of antibiotic action. In our studies a zone of 24 millimeters of inhibition corresponds to 100 units of antibiotic in each 100 cc. of material examined.

All pertinent studies, starting with those of Fleming, express the antibiotic action in units per cubic centimeter. We present our graphs in units per each 100 cc., as all humoral indexes are expressed and in this way the antibiotic action is expressed in whole numbers which are easier to handle than the decimal figures of the older method. Accordingly, all our graphs are made on millimeter paper, each millimeter equals one unit of antibiotic action per 100 cc. of the material tested (blood, sputum, etc.).

Clinical Considerations:

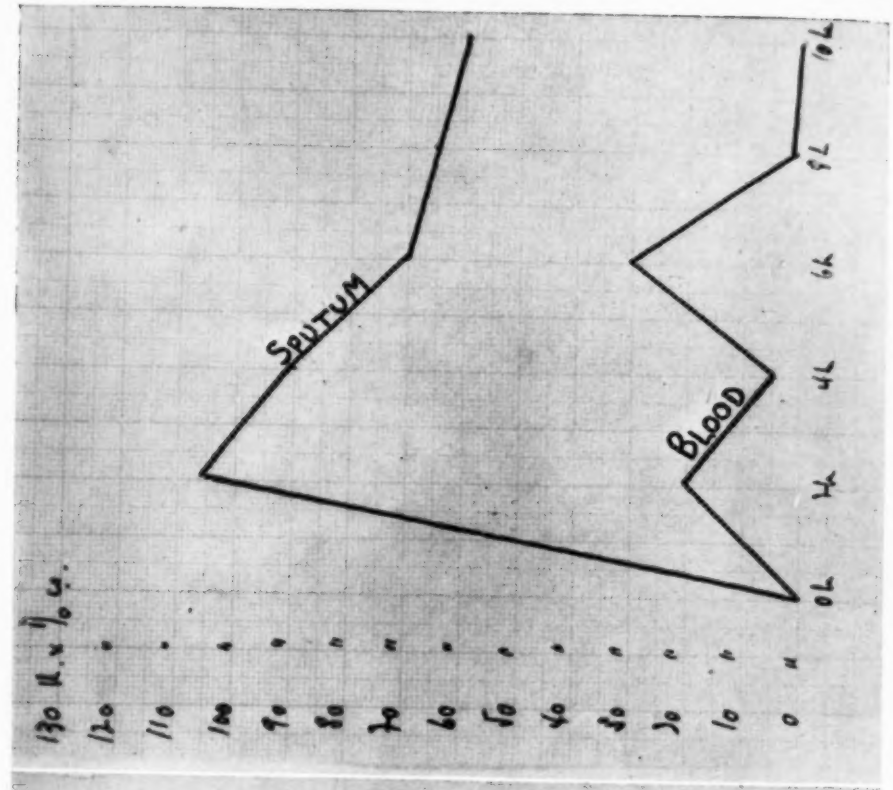
The cases selected were patients who formerly had received oral medication or antibiotics administered parenterally. During the trial of this method, intratracheal crystalline penicillin was used exclusively. No other antibiotic medication was employed at any other time.

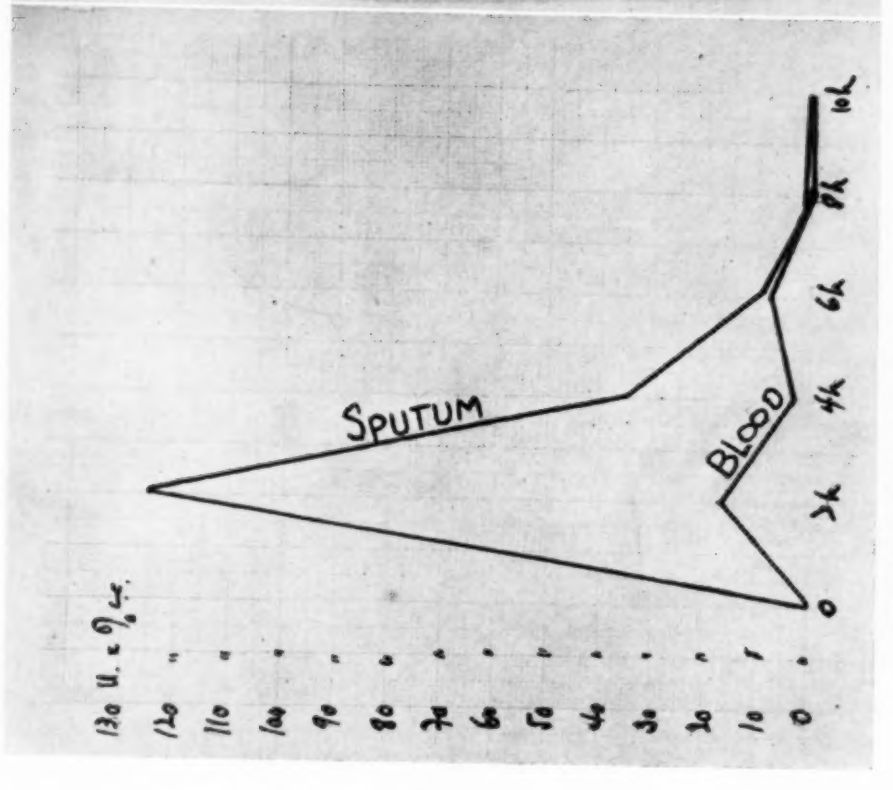
Among the cases selected, one patient had a neoplasm with abscess in the middle lobe of the right lung who entered the hospital for an operation. Before his admission to the hospital no diagnosis of lung tumor had been made and suspecting an abscess of the lung, high doses of penicillin were given simultaneously with sulfa drugs. There was no reduction in the amount of bronchial secretions which reached 300 cc. in 24 hours and were bloody and purulent. The patient was quite toxic, had moderate anemia with much cough, especially at night and a most aggravating dyspnea. The bronchoscopic examination did not show tracheobronchial lesions. Five intratracheal applications were given to him by our method, one every day, using crystalline penicillin in maximal doses of 400,000 units in each application and in solutions of 15 to 20 cc. of isotonic saline. We noticed in the first application a definite pharyngeal reflex. We obviated this in the following treatments by giving previously an injection of 1.0 mg. of morphine with atropine. Following the second application, the continuous coughing of the patient was relieved, the expectoration began to diminish and at the end of the fourth application it had come down to 15 cc. in 24 hours. The patient's general condition improved and his recovery was maintained for several weeks, when refusing surgical intervention, he left the hospital.

In bronchiectasis we have observed quick reduction of expectoration in 24 hours with a modification of the bacterial flora.

The graphic curve of concentration of antibiotic of sputum and blood simultaneously obtained in this group have been very interesting. We observed that the concentration of antibiotic in the blood was maintained during the first eight hours, fluctuating between 15 and 2 units per each 100 cc. In the sputum, in the same number of hours, the antibiotic action fluctuated between 125 and 35 units per each 100 cc. In case number 5 (Fig. 2), multiple bronchiectasis of both lung bases, using always 300,000 units of penicillin at a time, with our method a remarkable difference has been observed in the levels simultaneously obtained from sputum and blood.

In case number 2 (Fig. 3), abscess of the vertex of the lower lobe of the left lung cleared promptly under the effect of our treatment. This case, a 31 year old farmer, with a lung affection





FIGURES 2 and 3: Comparative concentration curves of the antibiotic action in sputum and blood.

of seven months' duration, was characterized by pain in the flank, high temperature, coughing, abundant purulent expectoration, with asthenia, loss of energy and anorexia. During his second month of illness sulfa drugs were given orally and penicillin parenterally, with no improvement in his condition. The physical examination showed a noticeable oral sepsis, "watch glass" nails and a condensation syndrome at the left-scapular-vertebral zone, with several subcrepitant rales. Mucopurulent sputum showed numerous pyogenic cocci. Its culture revealed the presence of staphylococcus aureus. There was slight anemia, with 15,000 leucocytes, young cells predominating. On bronchoscopic examination we found very fetid secretions originating from the left lower lobe bronchi.

In all, twenty-five intratracheal applications were made in this case, with maximum dose of 400,000 units of penicillin in a solution of 5 cc. of isotonic saline. After the fourth application we noticed that the expectoration diminished, coughing at night was less, his appetite and general condition improved. After every application the patient felt better and at the end of the first 20 applications his general condition was good. His expectoration, coughing, fever and asthenia had ceased. He had his normal weight. Nothing important was noticed in the physical examination of the chest. In the x-ray picture we only observed traces of the contrast medium used in the bronchographic examination (Fig. 4). In the final culture of the patient's sputum only catarrahlis cocci were observable (Fig. 5). Concentration of peni-

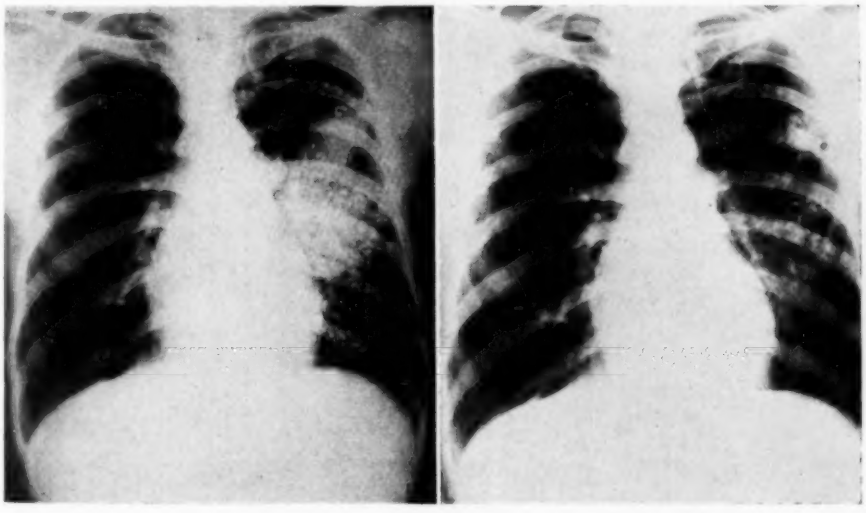


FIGURE 4 FIGURE 5

Fig. 4: Pulmonary abscess of the appex of the left lower lobe.
Fig. 5: One month later: Complete resorption of the process.

cillin in the blood and sputum curves during treatment was similar to those described in our former observation. This patient was kept in the hospital for several weeks after treatment, without observing any further clinical or radiographic manifestations of the infection.

SUMMARY AND CONCLUSIONS

1) We have used a technique developed by us for mucosography of the respiratory tract and applied to the treatment of suppurative diseases of the lung.

2) This preliminary report covers a group of cases treated with penicillin which we have used in different concentrations, between 100,000 and 500,000 units disolved in isotonic saline solution. The application was made daily with progressive increase in the doses of penicillin.

3) We preferred crystalline penicillin because it is better tolerated; the volume used has been 5 cc. Larger amounts show no advantage, for it delays the method, and the patient develops pharyngeal irritation.

4) It is an easy method to use, with no risk or disturbance to the patient. The amount of anesthesia used is very small, atomization of 2 cc. of ½ per cent pantocain solution is sufficient. In some patients we have sprayed without anesthesia, and noticed good tolerance.

5) We perform the atomization continuously. That is, in both phases of respiration, in order that the patient may keep open the glottis to avoid coughing and pharyngeal contractions.

6) We have used the supra and infraglottic technique. We prefer the supreglottic technique because it is better tolerated.

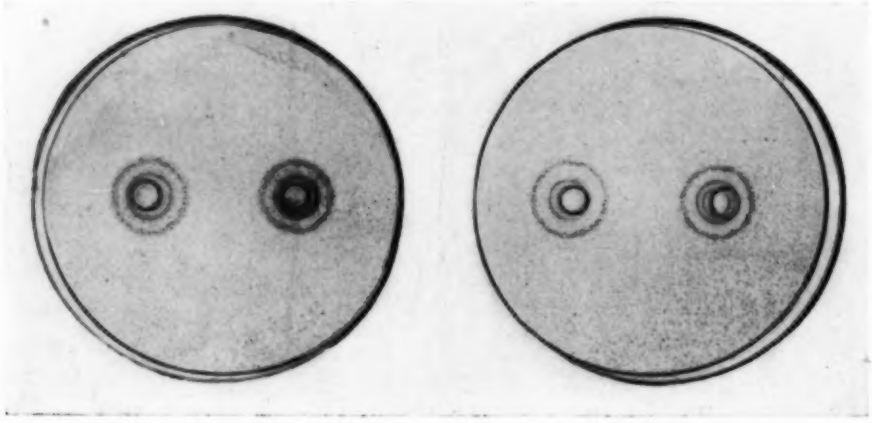


FIGURE 6: Petri dishes showing the different intensity of the antibiotic action of sputum and blood.

7) The results obtained are definately encouraging. We have succeeded in improving and curing suppurative lung conditions some of which were of more than six month's duration and having been previously treated without success with penicillin and sulfa drugs.

8) It is interesting to point out that the simultaneous study of sputum and blood in our patients shows high antibiotic action in the sputum and quite low antibiotic action in the blood. It is easy to see in our graphs that the antibiotic action of the sputum fluctuates between 130 units as maximum and 40 units as minimum, the antibiotic action of the blood fluctuates between 30 units as maximum and 2 units as minimum.

These facts bring forth certain questions which we shall try to explain:

(a) Does the high bacteriostatic power found in the sputum represent the whole penicillin concentration or is it related to any other antibiotic action?

(b) Does the high bacteriostatic action found correspond to acumulative or eliminative action?

(c) Do proteins of the expectoration (mucins, mucoids, etc.), have anything to do with the "delayed effect" in connection with the penicillin deposited in the bronchi?

9) The results obtained point toward the extraordinary importance of the topical action of antibiotics.

10) Finally, with this method we can direct to a certain pulmonary area the highest percentage in volume and concentration of the drug used, which, to our belief is not obtainable by any other method of inhalation used up to the present moment.

Atomizer described manufactured by the DeVilbiss Company.

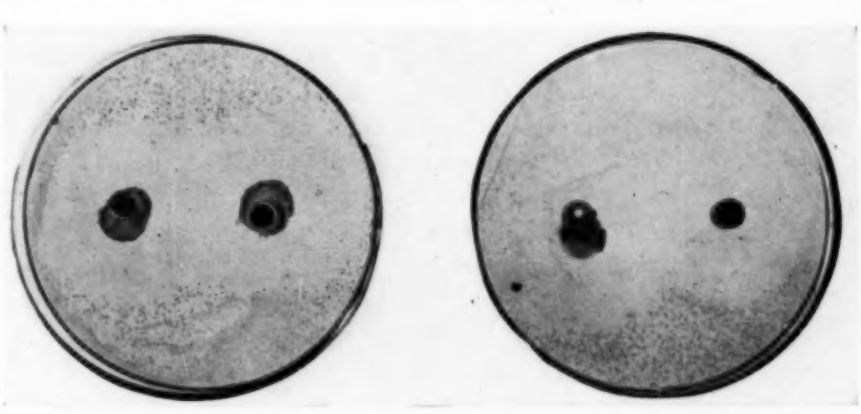


FIGURE 7: Petri dishes showing the different intensity of the antibiotic action of sputum and blood.

RESUMEN Y CONCLUSIONES

1) Hemos empleado una técnica perfeccionada por nosotros para la mucosografía del aparato respiratorio y aplicada al tratamiento de las enfermedades supuradas del pulmón.

2) Este informe preliminar incluye un grupo de casos que hemos tratado con penicilina en concentraciones de 100,000 a 500,000 unidades disueltas en una solución isotónica de cloruro de sodio. Se aplicó el tratamiento diariamente, con aumento progresivo en la dosis de penicilina.

3) Preferimos la penicilina cristalina porque es más tolerable. Se ha usado un volumen de 5 cc. Cantidades más grandes no ofrecen ventaja, pues demoran el método y el paciente sufre de irritación faríngea.

4) Es un método fácil de usar que no tiene peligro ni causa desasosiego al paciente. Es muy pequeña la cantidad de anestésico empleada, es suficiente la pulverización de 2 cc. de una solución de pontocaína al 0.5 por ciento. Hemos rociado sin anestesia a algunos pacientes y lo han soportado bien.

5) Ejecutamos la pulverización contínuamente, es decir, en las dos fases de la respiración, a fin de que el paciente mantenga la glotis abierta para evitar la tos y las contracciones faríngeas.

6) Hemos empleado la técnica supraglótica e infraglótica. Preferimos la técnica supraglótica porque es más tolerable.

7) Los resultados obtenidos son definitivamente alentadores. Hemos logrado la mejoría o la curación en estados supurados del pulmón, algunos de los cuales habían existido por más de seis meses y habían sido tratados previamente sin buen éxito con penicilina y sulfonamidas.

8) Es interesante indicar que, en nuestros pacientes, el estudio simultáneo del esputo y de la sangre demostró una acción antibiótica elevada en el esputo y una acción antibiótica bastante baja en la sangre. Se puede ver en nuestras gráficas que la acción antibiótica del esputo fluctúa entre 130 unidades como máximo y 40 unidades como mínimo, y la acción antibiótica de la sangre fluctúa entre 30 unidades como máximo y 2 unidades como mínimo.

Estos hechos sugieren ciertas preguntas que trataremos de contestar:

(a) ¿Representa el elevado poder bacteriostático del esputo la entera concentración de la penicilina, o está relacionado con alguna otra acción antibiótica?

(b) ¿Corresponde la elevada acción bacteriostática a una acción acumulativa o eliminativa?

(c) ¿Tienen algo que ver las proteínas de la expectoración (mucinas, mucoides, etc.) con el "efecto demorado" de la penicilina depositada en los bronquios?

9) Los resultados obtenidos demuestran la extraordinaria importancia de la acción tópica de los antibióticos.

10) Finalmente, con este método podemos aplicar a una zona pulmonar el porcentaje más alto, en volumen y en concentración, de la droga empleada, lo que, en nuestra opinión, no es obtenible mediante ningun otro método de inhalación usado hasta la actualidad.

Thrombosis of the Main Stem of the Pulmonary Artery Associated with Pulmonary Tuberculosis
Report of a Case

ALFRED W. KORNBLUTH, M.D. and
F. PAUL O'HARA, M.D., F.C.C.P., F.A.C.S.
San Diego, California

Savacool and Charr[1] in 1941, reviewed the literature for one hundred cases of pulmonary artery thrombosis of the main stem or its main branches. In their series of cases nineteen were reported to have had pulmonary tuberculosis as a primary diagnosis. Perusing the literature through to 1946 failed to disclose any further reports of pulmonary artery thrombosis.

The following case is reported because of its many interesting features and because of the diagnostic problem presented by the course and symptoms:

E.H., a thirty year old white housewife, entered the San Diego County General Hospital, Tuberculosis Division, on October 26, 1946, with pulmonary tuberculosis confirmed by roentgenograms and sputum containing acid fast bacilli. The patient had been essentially well until nine years before this entry when she first recalled noting dyspnea, with slight exertion, occasionally associated with cyanosis of her face and fingers.

At that time she was seen in the Out-Patient Department of the United States Naval Hospital, at San Diego, where a tentative diagnosis of congenital heart disease was made. Specifically, an interatrial septum defect was considered. Roentgenograms revealed an enlarged right auricle and pulmonary conus. There was a systolic murmur at the base of the heart on the left side of the sternum. The systemic blood pressure and physical examination at that time were otherwise within normal limits. The x-ray films taken on these visits are no longer available for re-examination.

The patient attended the clinic intermittently, noting a gradual increase in the severity and frequency of her symptoms. In February 1945, she entered the United States Naval Hospital following a sudden increase in the above symptoms plus an acute onset of fatigue, fever, sweating, cough and vague chest pain anteriorly.

Roentgenogram taken at that time (figure 1) showed an increase in the size of the upper mediastinal shadow with a bulging density in the region of the pulmonary conus on the left. There were scattered areas suggestive of atelectasis in the left lung field with almost complete atelectasis at the apex. There was also some enlargement of the hilar density on the right. The trachea, in the upper portion of the chest, deviated sharply to the right suggesting the effect of pressure from the mediastinum. The electrocardiogram revealed marked right axis deviation.

The possibility of bronchopneumonia or tuberculosis was considered at that time. Repeated examination of the sputum revealed no acid-fast bacilli and blood cultures on two occasions were negative. The patient was treated with sulfathiazole and required the use of an oxygen tent. Her acute symptoms gradually subsided, over a period of three weeks. The cardiac murmur and a daily afternoon spiking temperature to 101 degrees F. orally disappeared as her symptoms subsided. The patient was discharged one month after entry. The x-ray film taken at the time of her discharge showed a considerable amount of clearing of the process in the left lung field with essentially no other changes in the heart or vascular shadows. There was still some residual atelectasis present in the left apex.

Following her discharge from the hospital, the patient continued to note her previous complaints of occasional dyspnea and cynosis. On September 26, 1946, she had a re-check roentgenogram taken at the San Diego County Tuberculosis Clinic. This film revealed, on the right side, a fibrotic infiltration extending out from the hilar region into the second interspace with an area simulating cavitation at the end of the second rib anteriorly. The hilar markings showed some increase in their size and density. The left side revealed some increase in the density previously seen in the first and second interspaces with areas suspicious of cavitation. The contour of the heart and mediastinum were not apparently changed.

The sputum examined at that time was found to contain acid-fast bacilli. The patient entered Vauclain Home on October 26, 1946, following the establishment of the diagnosis of tuberculosis.

The past history included a full term normal delivery preceded by elevation of the blood pressure during the last trimester. She denied symptoms of heart trouble before 1937, joint pains or swelling, chorea,

FIGURE 1

FIGURE 2

tuberculosis contacts, venereal disease, or allergy. In the family there was no known case of congenital abnormalities or tuberculosis.

The physical examination on admission revealed a well developed, poorly nourished, cyanotic, dyspneic white female appearing older than her age and easily upset emotionally. Her temperature was normal, pulse 90 and regular, and respirations 22. Blood pressure readings were as follows: right arm 118/90, left arm 120/95, leg 110/90.

Positive findings included a lag in the excursion of the left side of the chest. Anteriorly, at the apex on the left, dulness with breath sounds decreased in intensity and bronchial in quality were noted. Posteriorly, at the left apex, dulness with bronchovesicular breath sounds and a few crepitant rales were heard. The heart was not enlarged to percussion and no murmurs, irregularities or thrills were present. P2 was louder than A2. One observer noted an apical, grade one systolic blowing murmur. Her fingers were exhibiting a moderate degree of clubbing.

The laboratory tests on admission were as follows: urine essentially negative; hemoglobin 103 per cent; WBC 6,600; leukocytes 72; lymphocytes 25; monocytes 3 per cent. The Kline and Wassermann tests were negative and the sputum contained acid-fast bacilli.

The roentgenogram, dated November 15, 1946 (figure 2) taken soon after admission, revealed no change on the right side. On the left side the density in the upper mediastinal region appeared somewhat larger and now simulated a tumor. The configuration of the heart was unchanged. The electrocardiogram revealed notching of the QRS waves in leads 2, 3 and 4, with inversion of the T waves in these same leads. The S wave was depressed in lead 1. These findings were interpreted as representing right axis deviation and right ventricular strain.

In January 1947, roentgenogram of the chest with ingestion of barium showed deviation of the esophagus to the right and posteriorly at the level of the fifth, sixth, seventh and eighth thoracic vertebrae, appar-

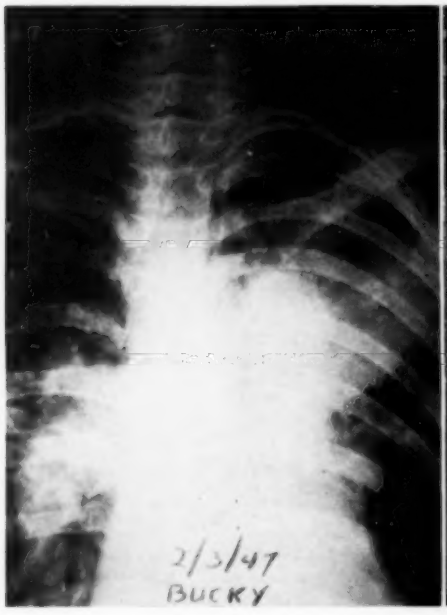


FIGURE 3

FIGURE 4

ently from extrinsic pressure. Surgery for a possible mediastinal or bronchogenic malignancy was considered at this time but was deferred because of the poor operative risk and prognosis for the patient with active tuberculous lesions in the lung parenchyma.

On February 3, 1947, a Bucky film (figure 3) showed an increase in the size of the density in the right hilar region, with soft infiltration extending out laterally. On the left side there was a fairly well circumscribed density in the upper portion of the hilar region giving the appearance of a tumor mass with a well defined area of atelectasis extending into the lower part of the upper lobe. The interpretation of this increased density was still not clear. During this time, while on bed rest, the patient gradually gained weight. She had an occasional late afternoon spiking temperature to 101 degrees F. orally. In April 1947, blood streaked sputum was noted for the first time. Cyanosis was still present and unchanged from that noted at the time of her admission.

On June 17, 1947, the patient felt a sudden pain in her left lower chest which increased in severity during the following three days. This pain was associated with fever, apprehension, increased pulse and cyanosis and the production of small quantities of dark red blood in the sputum. These symptoms, fluctuating in severity, continued until death. Physical examination at the time of the onset of these more severe symptoms revealed dulness over the left side of the chest with absent breath sounds and medium moist rales throughout the left lung field. An x-ray film taken of the chest on June 20, 1947 (figure 4) showed little change in the findings on the right side. The left side was obscured by a homogeneous density except at the extreme apex where some areation was visible. The heart and mediastinum were shifted to the left. The picture appeared to be that of atelectasis rather than pleural effusion. Attempts at aspiration of the left chest were unsuccessful. Bronchoscopy on July 23, 1947, revealed narrowing of the left main bronchus, apparently due to extrinsic pressure. The orifice of the left upper lobe bronchus could not be visualized. The bronchial mucosa was not remarkable.

In September, re-check laboratory findings included hemoglobin 138 per cent; RBC 7,550,000; WBC 9,750; lymphocytes 19; monocytes 5; eosinophils 1; leukocytes 75 per cent; hemotacrit 80 cc./100 cc.; blood urea nitrogen 24.1 mg. per 100 ml. On October 5, 1947, the circulation time from arm to tongue with gluco calcium was twenty-three seconds; from arm to lung with ether was ten seconds.

The patient continued in a gradual down hill course, becoming more dyspneic and less rational until October 7, 1947 when she expired with no apparent acute incident terminally. The temperature remained below 100 degrees F. and the pulse varied between 100 and 110. The respiratory rate was 20 to 25 per minute up to the time of her death. No peripheral edema or enlargement of the liver was noted. A roentgenogram taken just before death revealed no change in the left side of her chest, however, the lesion in the right midlung field appeared to have been clearing and hardening.

The postmortem examination revealed, in the thorax, old pleural adhesions bilaterally. The left lung showed scattered areas of atelectasis, especially in the upper lobe with multiple areas of active tuberculosis. The lower lobe was the sight of a massive infarct with thrombotic obstruction of the artery to this lobe. The right lung shodew multiple tuberculous lesions, especially at the apex, with a few scattered thromboses of the smaller pulmonary arteries. The heart presented the picture

of dilatation and hypertrophy of the right side. There was a large laminated antemortem thrombus apparently occluding the pulmonary stem and its two branches extending to the pulmonary semilunar valves. The thrombus was gray in color at the pulmonary artery branches, becoming red in color as it approached the pulmonary valve. The blood clot was firmly attached to the wall of the artery, but when separated there was a clean plane of cleavage with no gross evidence of disease of the large arteries. Unfortunately, no microscopic sections are available.

Discussion

At the onset of her symptoms this 20 year old woman sought medical attention for shortness of breath and blue discoloration of her fingertips. Upon examination cor pulmonale and a basal systolic murmur were found. In the absence of any evidence of pulmonary abnormality a tentative diagnosis of interatrial septum defect was made. Cardiac catheterization would have been of great value in ruling out patent foramen ovale and determining the pressure in the pulmonaray circulation which was undoubtedly elevated.

According to Brenner,[2] the above picture fulfills the criteria for a diagnosis of primary pulmonary vascular sclerosis. De Navasquez et al[3] question the significance of pulmonary vascular lesions in some cases of cor pulmonale due to pulmonary hypertension without apparent etiology and propose the term idiopathic right ventricular hypertrophy. Taft and Mallory[4] believe that this pulmonary hypertension of unknown etiology probably precedes sclerotic changes in the pulmonary vessels. In the absence of any evidence of left heart failure, the markedly prolonged circulation time from arm to tongue as compared to the only slightly prolonged circulation time from arm to lung, point to some peripheral vascular disease in the pulmonary circulation. Brill and Krygier[5] emphasize the significance of cyanosis that is out of proportion to the amount of dyspnea as being an outstandingly frequent finding in pulmonary vascular disease, particularly pulmonary vascular sclerosis. This picture was an outstanding feature of the patients symptoms, nevertheless that diagnosis remains in the realm of speculation.

In retrospect, therefore, it appears that the patient when first seen had cor pulmonale due to pulmonary hypertension of unknown etiology, possibly due to pulmonary vascular sclerosis.

The acute episode requiring hospitalization in 1945 was considered at that time to be due to a pneumonitis in the left upper lobe complicating a congenital heart disease. Because of the similarity of the roentgenograms taken at the United States Naval Hospital and those taken on admission to Vauclain Home, it is interesting to speculate whether or not the patient had

tuberculosis and/or atelectasis in the left upper lobe in 1945. The former may have been present in spite of repeatedly negative sputa examinations for acid fast bacilli. The latter could have been due to pressure on bronchi by pulmonary vascular thrombi originating at that time.

The time of origin of the pulmonary thrombus raises another point for speculation. The thormbus may have formed in 1945 at the United States Naval Hospital, resulting in atelectasis as pointed out above. On the other hand, this process may not have started until after entry into Vauclain Home where the embarrassed cardio-pulmonary dynamics complicated by tuberculosis in a bed ridden patient may have set the stage for the onset of the process of thrombus formation.

The authors feel that the patient at the time of her first hospitalization, in February 1945, probably had tuberculosis and atelectasis following the onset of the thrombosis. This thrombus continued to grow until the impairment of the blood supply to the left lower lobe was sufficient enough to result in the infarct which occurred in June 1947. Life was maintained until the heart became unable to stand the strain of pumping blood through the pulmonary arterial system so massively thrombosed.

In Dock's[6] explanation of the localization of phthisis he points out that the incidence of apical or subapical lesions of tuberculosis is higher in patients with pulmonary hypotension as compared to the incidence in patients with pulmonary hypertension. This is not inconsistent with the course of events in this case, for the formation of the thrombus in the pulmonary artery may have been expected to have materially decreased the effective pulmonary arterial pressure. This, according to Dock, decreases the oxygenation and impairs function of humoral defenses in the body.

That the thrombosis occurred first in the left pulmonary artery is suggested by the fact that the first changes noted in the lungs were found on the left. Savacool and Charr[1] in their series of 100 cases report only six cases which were interpreted as having thrombosis of the left main branch only or origin of the thrombus in this branch of the pulmonary artery. The relative infrequency of this finding was explained by the longer and more tortous course of the right as compared to that of the left branch of the pulmonary artery.

SUMMARY

An interesting case of thrombosis of the pulmonary artery stem and its main branches in a patient with pulmonary tuberculosis is presented with a discussion of the pertinent findings and observations.

RESUMEN

Se presenta un caso interesante de trombosis de la arteria pulmonar y sus ramas principales en un paciente con tuberculosis pulmonar y se discuten los hallazgos y observaciones pertinentes.

REFERENCES

1 Savacool, J. W. and Charr, R.: "Thrombosis of the Pulmonary Artery," *Am. Rev. Tuberc.*, 44:42, 1941.
2 Brenner, O.: "Pathology of Vessels of the Pulmonary Circulation," *Arch. Int. Med.*, 56:457, 1935.
3 de Navasquez, S., Forbes, J. R. and Holling, H. E.: "Right Ventricular Hypertrophy of Unknown Origin," *Brit. Heart J.*, 2:177, 1940.
4 Taft, E. B. and Mallory, K. G.: "Primary Pulmonary Vascular Sclerosis," *Arch. Path.*, 44:630, 1946.
5 Brill, L. C. and Krygier, J. J.: "Primary Pulmonary Vascular Sclerosis," *Arch. Int. Med.*, 68:560, 1941.
6 Dock, W.: "Apical Localization of Phthisis," *Am. Rev. Tuberc.*, 53:297, 1946.

Platybasia Associated with an Unusual Case of Pulmonary Tuberculosis

Report of a Case with Necropsy*

ISAAC EPSTEIN, M.D., F.C.C.P.
Alexandria, Louisiana

Chamberlain's paper in 1939 on "Basilar impression (platybasia)"[1] has stimulated the interest of the medical profession in the study of malformation of the base of the skull and upper cervical spine, an anomaly up to that time receiving very little attention. In this paper he proposed a criterion for the diagnosis of platybasia based on the amount of projection of the odontoid process above a line drawn on a conventional lateral x-ray film of the skull connecting the posterior edge of the hard palate to the dorsal margin of the foramen magnum; the line now being referred to as "Chamberlain's line." Two cases in Chamberlain's[1] series were treated by low occipital craniectomy and laminectomy of cervical segments with definite subjective and clinical improvement of their neurological symptoms.

According to Schueller,[3] on the other hand, the diagnostic features of platybasia are the cephalad bulging of the floor of the posterior cranial fossa around the foramen magnum and the congenital variations of the upper cervical vertebrae.

The case described in this paper is a bizarre one, not only because of the presence of the developmental anomaly of the occipital bone and upper cervical portion of the spinal column, but also in the clinical course of the pulmonary tuberculous disease with its unusual concomitant complications.

Case Report with Necropsy Findings

J.C.B., No. 47,620, colored male, aged 25, was admitted to the Veterans Administration Hospital, Alexandria, Louisiana, on December 23, 1946, for treatment of pulmonary tuberculosis. In addition to the usual symptoms of pulmonary tuberculosis, the patient presented the following neurological findings: Excessive sweating limited to the entire left half of his body, fleeting joint pains, loss of the sense of differentiation between cold and heat, and dull and sharp, on the left side. The gait was staggering and unsteady but there was no history of trauma to the head or spine and at no time was there a loss of consciousness or convulsion.

The physical examination disclosed a well developed and well nourished colored male who appeared chronically ill. The temperature, pulse, and respirations were within normal limits and the blood pressure was 120/80.

---

*From the Chest Service, Veterans Administration Hospital, Alexandria, Louisiana.

Examination of the chest revealed signs of a bilateral involvement with coarse post-tussive rales scattered throughout the middle portions and bases of both lungs. The above findings were confirmed by x-ray examination of the chest. Routine sputum examinations were consistently reported positive for acid fast organisms. Urine and Wassermann examinations were negative. Sedimentation index was 30 mm. in one hour. Complete blood count revealed: Hemoglobin 61.4 per cent, Red Blood Count 3,670,000, White Blood Count 8,200 Polymorphonuclears 60 per cent, Lymphocytes 38 per cent and Basophiles 2 per cent, Urea nitrogen 13, Cholesterol 120 and basal metabolism ranging from plus 1.9 to 19 per cent.

The Therapy Board recommended that patient be observed for a period of 30 to 60 days. During this period the author bronchoscoped the patient and aspirated a large amount of mucopurulent secretion from both main bronchi, finding no evidence of ulceration or stenosis of the bronchi. The patient's pulmonary condition, however, had not improved on routine management. Subsequent roentgenogram of the chest revealed a definite increase in the lesions in both lung fields and cavitation in the middle portions near the hilar region. Pneumoperitoneum was induced on March 25, 1947.

A transient improvement in patient's clinical and radiological condition was noted under this treatment, but the disease apparently was not controlled. In fact, the patient developed further cavities in the 2nd interspace on the left side and started to hemorrhage (Fig. 1). It was decided at this time to induce pneumothorax on the left side in addition to the pneumoabdomen. Patient's vital capacity (2,800 cc.), checked prior to inducing pneumothorax on the left side appeared very satisfactory. Electrocardiogram on September 22, 1947 showed sinus tachycardia but no definite cardiac pathology contraindicating combined pneumoabdomen with pneumothorax therapy. Initial treatment of 150 cc. of air,

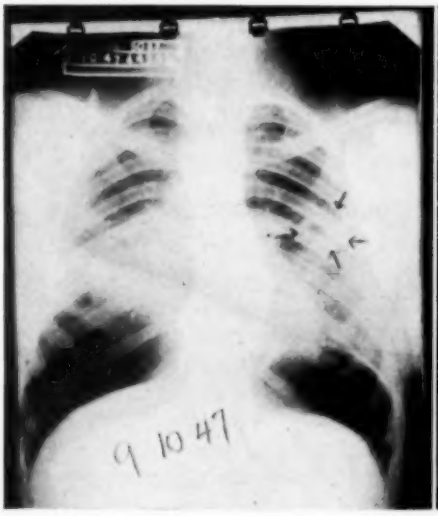


FIGURE 1

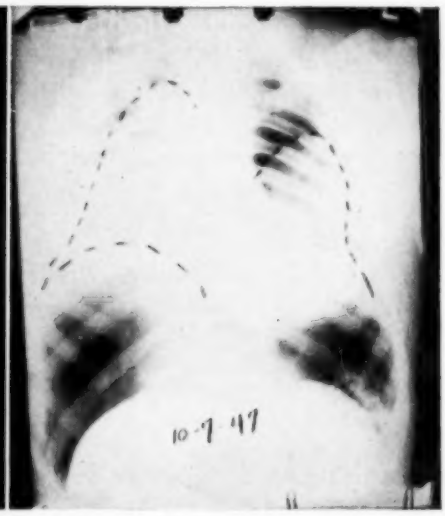


FIGURE 2

Fig. 1: Roentgenogram of the chest taken September 10, 1947, shows marked elevation of the diaphragms and a huge cavity in the 2nd interspace on the left side.—*Fig. 2:* Roentgenogram of the chest taken October 7, 1947, shows a collapse of both lungs in addition to an extensive pneumoabdomen.

under high negative pressure, was given on the left side on September 26, 1947 without any ill effect.

On October 8, 1947 without any obvious cause, the patient's temperature rose to 104.4° F. with a pulse rate up to 120 per minute and respirations of only 22 per minute. The patient was lying in bed quietly but complained of some fleeting pain in his shoulder joint and his left arm. There was no evidence of respiratory distress, nor any orthopnea.

Examination of the chest, including fluoroscopy, revealed collapse of both lungs with marked elevation of the domes of the diaphragm due to pneumoperitoneum. In other words, this patient had developed a spontaneous collapse of his right lung without noticeable dyspnea (Fig. 2). Continuous deflation was started immediately on the right side and patient was placed in an oxygen tent. The following day deflation was stopped because the air was not bubbling through the water trap. The possibility of continuing bilateral pneumothorax was then contemplated, provided that we were not dealing with a congenital mediastinal defect.[2] It was noteworthy that while this patient's temperature was markedly elevated, up to 105° F., with a pulse of 136, his respiratory rate, nevertheless, was of usual frequency, only 18 to 24 per minute, a marked discrepancy between his respirations and his total clinical condition. The patient expired unexpectedly on October 12, 1947.

During the period of hospitalization he continued to have bizarre neurological complaints. The neurological examination disclosed the following positive findings: Pupils central and unequal, the right pupil being smaller; a rotary nystagmus bilaterally which became more pronounced on gazing toward the right temporal side; cremasteric reflex absent on the left side; knee and ankle jerks hyperactive on the right side; deep reflexes on the left side markedly diminished; definite sensory changes from the level of the left nipple down and marked sweating of the entire left half of the body.

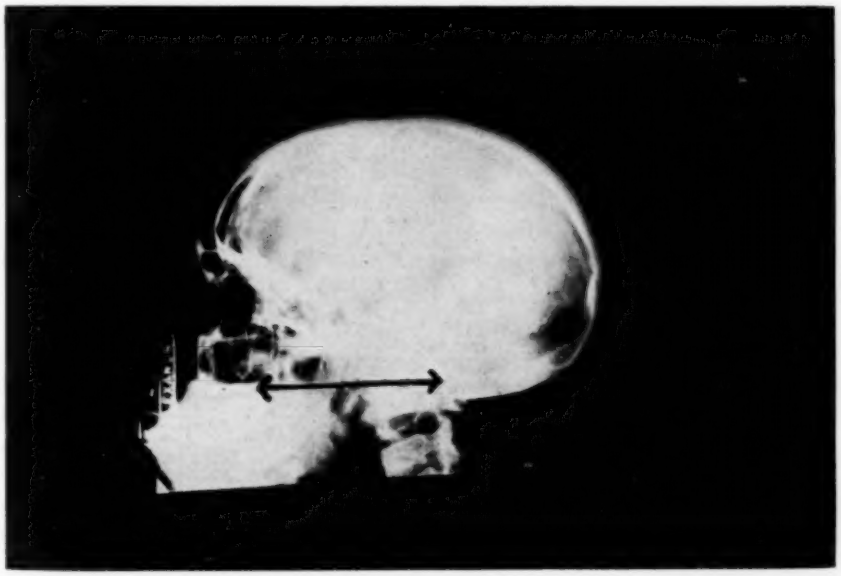


FIGURE 3: Roentgenogram of the skull shows projection of the odontoid process above the line drawn from the posterior margin of the hard palate to the posterior lip of the foramen magnum.

These neurological symptoms were suggestive of syringomyelia. The x-ray of the skull (Fig. 3), however, showed a flattened and stenosed foramen magnum and projection of the odontoid process well above the "Chamberlain's line," consequently the diagnosis of platybasia was made.

The pertinent postmortem findings were as follows: There was narrowing of the foramen magnum in the antero-posterior diameter and there was elevation of its edge at the anterior rim. The exact anatomy of the atlas and second cervical vertebra was not explored to avoid mutilating the body. There was no protruberance of the cerebellar tonsils through the foramen magnum. The lung findings were in accordance with those demonstrated by x-ray. No demonstrable interpleural communication was present. Histologically nothing of significance was found except for chromatolytic changes in occasional anterior horn cells.

Comment

No other case of pulmonary tuberculosis associated with basilar invagination is to be found in the medical literature. The relationship is coincidental but the neurological changes appear to have masked many of the patient's pulmonary symptoms. The discrepancy between the slow respiratory rate and the febrile clinical course was striking during the entire period of hospitalization.

There is a possibility that we are dealing here with more than one congenital anomaly, both a mediastinal defect and platybasia. This is evidenced by the fact that this patient after the fourth injection of air into his left side developed a spontaneous pneumothorax on the right side without its usual symptoms. The question arose: was there a very slow leakage of air through the mediastinum? This question is impossible to answer positively, because the patient did not survive long enough to permit proof of the defect in the mediastinum. The fact that a mediastinal opening could not be found at autopsy does not rule out its presence because others, such as Smith and Willis,[4] also could not demonstrate the mediastinal defect at autopsy in a proven case of interpleural communication during patient's life.

Our case had a bilateral pneumothorax with collapse of both lungs up to 60 per cent in addition to an extensive pneumoperitoneum, a combination rarely observed in tuberculous patients. There was no noticeable dyspnea at any time in this case which could be attributed to pressure on the respiratory center by some pathological process depressing the respirations. At necropsy there was no demonstrable impression on the medulla or the upper cervical cord due to pressure; nevertheless, histologically there was occasional anterior horn cell chromatolysis signifying a possible degenerative process.

Finally it would not be amiss to stress the fact that thorough search of the skull and cervical spine, especially roentgenolog-

ically, in all suspected cases of spinal cord degeneration showing symptoms of syringomyelia, multiple sclerosis, or other unusual patterns, might disclose many more cases of platybasia.

SUMMARY

1) Platybasia associated with an unusual case of pulmonary tuberculosis is reported and the possibility of a congenital mediastinal defect is also discussed.

2) The basilary invagination in this case apparently influenced the respiratory center by a depressing effect on the response of the respiratory rate to stimulation.

3) It is advisable that careful search for platybasia be made in every case with degenerative changes of the spinal cord.

4) The necropsy in this case confirmed our clinical diagnoses of platybasia and pulmonary tuberculosis with bilateral pneumothorax and pneumoperitoneum.

RESUMEN

1) Se informa sobre un caso de platibasia asociada con tuberculosis pulmonar inusitada y se discute también la posibilidad de que existiera un defecto congénito del mediastino.

2) En este caso la invaginación basilar aparentemente influenció el centro respiratorio y causó un efecto depresivo sobre la respuesta a la estimulación de la velocidad respiratoria.

3) Es prudente que se investigue cuidadosamente la existencia de platibasia en todo caso que presente alteraciones degenerativas en la médula espinal.

4) Es este caso la autopsia confirmó nuestros diagnósticos clínicos de platibasia y tuberculosis pulmonar con neumotórax bilateral y neumoperitoneo.

REFERENCES

1 Chamberlain, W. E.: "Basilar Impression (Platybasia)," *Yale J. Biol. and Med.*, 11:487, 1939.

2 Epstein, I.: "Mediastinal Defect with Interpleural Communication, Observed During Pneumothorax Therapy," Accepted for publication in *Diseases of the Chest.*

3 Schueller, A.: "Zur Roentgen-Diagnose der basalen Impression des Schadels," *Wien. Med. Wochschr.*, 61:2593, 1911 (quoted by Walsh).

4 Smith, C. R. and Willis, H. S.: "Communication Between the Pleural Sacs, With Lungs Showing Tuberculosis Healed after Thoracoplasty," *J.A.M.A.*, 101:1224, 1933.

Tuberculosis Among Medical and Academic Students

H. D. LEES, M.D.*
Philadelphia, Pennsylvania

The problem of tuberculosis among college students has been given careful study at many universities and colleges during recent years. The Tuberculosis Committee of the American Student Health Association has reported each year since 1932 on the tuberculosis activities of a large number of institutions located in all sections of the country. Through assistance rendered by the National Tuberculosis Association, the committee contacts each year all accredited colleges in the nation, approximately 880 in number. More than 300 colleges, having a total enrollment of approximately a half million students, are now conducting case finding programs. The detailed reports from these institutions provide a quite accurate picture of the prevalence of tuberculous infection and tuberculous disease among our student population.

A continuous program of tuberculosis control has been conducted among students at the University of Pennsylvania since 1931. Normal enrollment of full time students has averaged approximately 6,000. During the 15 year period under review in this report, our case finding activities have been directed as follows: the tuberculin test is applied routinely to all entering men students at the time of the required entrance physical examination. Reactors have chest x-ray inspection within approximately two weeks of enrollment. Entering women students, about 200 in number, are x-rayed without preliminary testing. Upper classmen are urged to have chest films annually. Although this is on a voluntary basis, the response has been excellent. X-ray surveys are conducted at the beginning and toward the close of each school year. A required program has been in effect for three groups of students since the inception of our case finding activities in 1931. Medical students receive especially close supervision throughout all four years of training. At entrance to medical school all students are tested with tuberculin by the Mantoux method employing the two standard doses and each student has a chest x-ray, non-reactors as well as reactors. Non-reactors are retested twice during each medical school year and chest x-rays are provided

*From the Department of Student Health, University of Pennsylvania.

for all reactors on an annual basis. During the present school year this plan was revised and now includes retesting of all non-reactors at intervals of two months and chest x-rays for all reactors during the school year. Athletes have also been rather carefully supervised at Pennsylvania. All members of varsity teams competing in intercollegiate athletics are required to have an annual chest x-ray. There are approximately 300 students participating on various athletic teams. The number of athletes found to have significant pulmonary lesions has provided rather convincing evidence of the need for adequate case finding procedures in such a group. The School of Education has also cooperated in a required program whereby their students are x-rayed at the time of entrance and again just prior to graduation. Since all of these young people are presumably entering the teaching profession shortly after graduation, it is important that we rule out the possibility of their being a source of infection in the classroom. The entire cost of the tuberculosis program is financed by a student health fee of five dollars a semester. Approximately 40 to 45 per cent of our students receive chest roentgenograms each year at a total cost of about three thousand dollars. This represents 5 per cent of the department's annual budget and, we believe, is an entirely reasonable expenditure in view of the significance of the tuberculosis problem among young adults of college age. Although the program outlined above assures quite adequate protection for certain large segments of our student body, a considerable proportion of upper class students do not report for follow-up studies each year as we urge them to do.

The incidence of tuberculous infection among college students has showed a steady and significant decline since 1932 when seven colleges reported that 35 per cent of their students were reactors to tuberculin. In 1942-43, among 42,107 students tested at 51 institutions, where at least an intermediate dose of tuberculin was employed, 18.6 per cent were reactors. In that year, thirteen colleges reported the incidence of infection among their students to be less than 10 per cent. Most of these institutions were located in midwestern and northwestern states. It has been shown by Long[1] that a higher incidence of infection prevails among students living on the East and West Coasts than among those in other sections of the country.

At the University of Pennsylvania 48 per cent of the students entering in 1931 were positive to tuberculin whereas the entering class in 1946 showed but 28 per cent to be reactors. This is especially significant in view of the fact that the average age of students making up the 1946 entering class is considerably above that of students entering fifteen years ago. This is accounted for by the

large number of veterans who are now enrolling in our colleges, many of them having been in service for a period of from one to four years. The incidence of tuberculous infection in this group has been somewhat lower than we had anticipated. Although our experience in this connection has been based on a relatively small number of veterans, approximately 4,000, it would appear that men in various branches of the service were, as a group, not unduly exposed to tuberculous infection. The picture might well have been quite different had routine chest x-rays been omitted from the medical examination at the time of induction.

During the past fifteen years a total of 177 students at the University of Pennsylvania has been found to have pulmonary tuberculosis. Of this number, 91 cases of the disease were among medical students and 86 cases were distributed among the students of all other schools. Since medical students comprised but 9 per cent of our total enrollment during this period, it is readily apparent that tuberculosis has presented a special problem to our students of medicine.

Among students on the undergraduate level, with an average age of approximately twenty years, reports from a large number of colleges over a period of years indicate the prevalence of pulmonary tuberculosis to be approximately 2 to 3 cases per thousand. At the University of Pennsylvania we have found approximately 5.7 cases of tuberculosis per thousand students exclusive of those in medical school. This rate applies to the entire non-medical group, including those in the undergraduate schools as well as students of law, dentistry and veterinary medicine. Of the 86 non-medical students found to have pulmonary lesions, 82.9 per cent were classified as minimal, 13.8 per cent were moderately advanced and 3.3 per cent were far advanced. The majority of this group presented lesions which were unstable. In all such cases, leave of absence is recommended and adequate treatment is advised. Readmission to the university is contingent upon evidence of satisfactory treatment and clinical and x-ray evidence of a presumably stabilized lesion. The value of a continuous program of tuberculosis case finding has been amply demonstrated by our experience at the University of Pennsylvania. Early diagnosis is of utmost importance if we are to prevent prolonged disability as well as unnecessary deaths. Only 6 of the 86 students found to have tuberculosis have failed to complete their education on our campus. This is largely due to the excellent and intelligent cooperation which we meet so consistently in dealing with college students. A large number of colleges and universities have had similar experiences. The report of the Tuberculosis Committee of the American Student Health Association for the academic

year 1941-42 shows that 744 new student cases of tuberculosis were discovered at 311 colleges which conducted programs of tuberculosis control. During that year, 319 students resumed their college work having undergone treatment for tuberculosis previously detected at these institutions.

Due to recent technical advances in the x-ray field the cost of surveying a student group has been reduced to a moderate level. With the incidence of tuberculous infection among students being below 30 per cent in most communities, it is of course a distinct economy to use the tuberculin test as a screening method and thus identify those who are infected with tubercle bacilli. Where tuberculin is applied by the Mantoux method employing either PPD or Old Tuberculin, it is quite well established that very rarely indeed will a person with significant tuberculous disease fail to react to the test. Furcolow, Hewell, Nelson and Palmer[2] report that in a series of over 500 cases of tuberculosis, in which they employed graded doses of PPD, more than 99 per cent reacted to the relatively small dose of 0.0001 mg. This is but five times the concentration of the usual first testing dose. They found none of the patients with active tuberculosis to be anergic to tuberculin. Long[3] of the Henry Phipps Institute has also emphasized the constancy with which persons having significant tuberculous disease respond to the tuberculin test. Among 610 cases of pulmonary tuberculosis diagnosed at the Institute during a five year period, only one of this number was a non-reactor. It is noteworthy also that among the 609 reactors, all of whom presented pulmonary lesions, 94 per cent of the white and 96 per cent of the colored patients reacted to the first small dose. A college is therefore justified in limiting chest x-rays to the reactors among their students if costs are an essential consideration. An adequate program of tuberculosis control is therefore available to most colleges, through use of the tuberculin test and x-ray of all reactors, at a cost which should not exceed three hundred and fifty dollars per thousand students.

The problem of tuberculosis among medical students has been rather carefully studied at a number of medical schools both in this country and abroad. Soper and Amberson[4] presented a very complete review of the subject in 1939. The earlier reports in the literature provide quite conclusive evidence that the incidence of tuberculosis in medical students is appreciably higher than in various other groups of comparable age. More recently, investigators have attempted to identify those phases of medical training which may be attended by definite risks of infection and to institute adequate control measures against all possible sources of infection. Several medical schools have succeeded in this manner

in reducing substantially the attack rates of both tuberculous infection and disease.

During the past fifteen years 91 medical students at the University of Pennsylvania have been found to have pulmonary tuberculosis among a total of approximately 2,300 students observed during this period. Ten students entered with lesions, thus 81 developed tuberculosis during their medical school training. In 90.1 per cent of students the disease was minimal, in 8.8 per cent it was moderately advanced and in 1.1 per cent it was far advanced. In addition to those presenting parenchymal lesions, there were five students who developed serofibrinous pleurisy. In our experience, tuberculous pleurisy with effusion has developed quite uniformly at approximately five to seven months after the date of primary infection. In all such cases the student is granted a leave of absence for one year and adequate bed rest treatment over a period of months is insisted upon.

The year of medical training in which tuberculous lesions have been detected in our students has followed much the same pattern as reported by other schools. The senior year has accounted for 38.6 per cent of cases, the junior year 49.1 per cent and 12.3 per cent have been found among second year students. The prevalence of tuberculous infection among students entering medical school has shown a decrease in recent years similar to that observed in academic freshmen. In the class entering in 1935 there were 66 per cent reactors to tuberculin, in 1939 there were 59.4 per cent and in the 1946 class 45.0 per cent. Morris[5] reports 58 per cent of medical students as reactors in the entering class of 1932 and 26 per cent reactors in 1940.

In studying the epidemiology of tuberculosis in medical students, nurses and similar groups, the tuberculin test has proved to be of indispensable value. If applied at sufficiently frequent intervals the approximate time of primary infection may be quite definitely established. High infection rates during certain limited periods of training are indicative of an environment which provides undue opportunity for infection. Various reports on the incidence of tuberculous infection in medical students and nurses indicates almost without exception a rate of increase from year to year which is well above that of the general population. Boynton[6] compared the incidence of infection in students in the college of education, student nurses on a general hospital service and student nurses on a special tuberculosis service. The infection rate was 100 times as great in those on a general hospital service as in college of education students and 500 times greater among those on a tuberculosis service. In the large general hospitals of our eastern cities a very high percentage of non-reactors among

nurses acquire infection during training. Israel, Hetherington and Ord[7] report on their observation of 637 nurses followed through three years of training at the Philadelphia General Hospital. Of 277 non-reactors on admission to training, 48 per cent became reactors during the first four months. By the end of the third year all of the originally negative group had become positive. Sixty-eight nurses or 10.6 per cent developed tuberculosis. At Bellevue Hospital in New York, Riggins and Amberson[8] found that close to 90 per cent of non-reactors among nurses converted during their three years of training. Up until quite recently there were but two or three members of each of our senior classes in medicine who remained negative to tuberculin up to the time of graduation. In 1945-46 however, the picture was as follows: Fourth year, 70 per cent reactors, third year, 64.4 per cent; second year, 55.8 per cent, and first year, 43.6 per cent. A recent report by Brean and Kane[9] dealing with tuberculosis among Harvard Medical School students presents several features of interest. In the 1932 entering class, 78 per cent of the students were tuberculin reactors whereas in the 1944 class there were 45 per cent reactors. During the period 1940-45 the attack rate of tuberculous infection was practically the same for students of all academic years, 12 to 13 per cent annually. The incidence of pulmonary tuberculosis in the medical classes of 1926 to 1932, during which period there was no organized case-finding program, was 0.9 per cent. Following the adoption of a program providing for routine tuberculin testing and annual x-ray of reactors, the classes of 1937 to 1943 showed an incidence of tuberculosis of 2.2 per cent. Their observations relative to the development of tuberculosis among those entering as reactors as compared with non-reactors led them to conclude that "the nature of the tuberculin reaction on entry had little influence on the development of active pulmonary tuberculosis in medical schools." They emphasize the need for continuous and adequate supervision of young adult groups who may have repeated contacts with tuberculosis by the following observation: "The adoption of a program in which surveys are made at intervals more frequent than once a year led to the elimination of almost all symptom-detected cases and of all major lesions. It is our belief that a semiannual examination represents the maximum interval for routine re-examination by x-ray and tuberculin tests, not only for medical students but also for nurses and interns."

During the past ten years the annual attack rate of pulmonary tuberculosis among our medical students has varied between 2.1 per cent and 0.38 per cent. The higher rate is based on 11 new cases discovered in 1938-39 while the lower rate prevalied in each of the last two years, with two new cases in each year. During

this ten year period 57 students developed tuberculosis among 1,700 students under observation, an incidence of 3.3 per cent. The last six years, however, have witnessed considerable improvement, the incidence during this period being 1.8 per cent. The lowered rates of infection and disease during the past few years have followed the adoption of various measures planned by a faculty committee after careful study of the problem over a period of years.

The various clinical and laboratory courses which have been considered at various schools as potential sources of infection to students are the following: Medical clinics, where known, open cases of tuberculosis are used for clinical teaching; physical diagnosis instruction, employing advanced cases of tuberculosis for the demonstration of abnormal physical signs; the pathology laboratory, in the demonstration and examination of gross specimens and the autopsy room with repeated attendance at necropsies on tuberculous subjects; the bacteriology laboratory, if work with virulent tubercle bacilli is required. There are also, of course, casual contact exposures which may be encountered during the clinical years through examination of undiagnosed cases of tuberculosis on various ward services and in the out-patient departments. At Pennsylvania we have attempted to reduce by every possible means the exposure of students to known sources of infection. It was observed that new lesions were detected in third year students more frequently than in other classes. And since most of these were discovered during the first few weeks of the school year, it seemed obvious that if the disease were due to superinfection from exogenous sources, such infection had probably occurred some months previously. Our records showed that there was a significantly higher conversion rate among second year students than among students of other classes. It was apparent, therefore, that the second year offered at least somewhat greater opportunity for reinfection than any of the other three years. Activities in the second year of medicine which provided possible contacts with tubercle bacilli were chiefly the courses in physical diagnosis and in pathology. In the former it was not unusual for students to spend repeated and prolonged sessions in the examination of patients with advanced tuberculosis. This practice has been discontinued. The department of pathology now uses only fixed specimens for laboratory demonstrations. Autopsy room technique was given careful consideration and several changes made for the protection of students. These included more adequate facilities for the washing of hands and the immediate discarding of contaminated gloves, gowns, and aprons.

Hedvall,[10] of Lund University, observed the frequency with which

primary infection in medical students coincided with the course in general pathology. Thorough and repeated examinations of autopsy rooms were made for the presence of tubercle bacilli. He reports that "in spite of all precautions as regards cleanliness during the post-mortem examination, tubercle bacilli were discovered in the rooms and on different objects when an examination was made twenty four hours after a necropsy examination of a person with tuberculosis." More stringent precautions for disinfecting autopsy rooms were taken and the number of autopsies attended by students was greatly reduced. Following the adoption of this plan they found that for the first time in their experience "all students who were non-reactors at the beginning of the course were also negative at the conclusion of the course." This observation, however, covered only two classes which completed the course under the new plan of reduced exposure.

Meade[11] of the University of Rochester Medical School recently reported a very thorough study of this problem and a program for its correction which has proved to be highly effective. Before instituting a case finding program in 1937, the known annual incidence of tuberculosis among their students was 0.9 per cent. By October 1941 their program provided for routine chest x-rays three times during the school year and in March 1943 tuberculin testing and chest x-rays were stepped up to four times a year. The average annual incidence of disease for the period 1937-42 was found to be 3.2 per cent, with a high of 5.0 per cent being reached in the school year 1939-40. Their investigation of probable sources of infection revealed that over a period of years an average of 52 per cent of students were reactors to tuberculin at the beginning of the second year whereas 91 per cent were reactors at the completion of the year. Thus 81 per cent of non-reactors acquired primary infection during the second year of the medical course. The only courses offered during this period in which students had known contact with tubercle bacilli were bacteriology and pathology. They felt that the former offered little, if any, degree of risk. With the cooperation of the department of pathology it was therefore agreed upon to eliminate all contacts with tuberculous materials in autopsy rooms and laboratories during a trial period. The program provided that no student would participate in known tuberculous autopsies; that students were to be dismissed from participation as soon as unsuspected tuberculosis was found at autopsy and no tuberculous materials were to be handled by them. Following the adoption of this policy most striking reductions were observed in both infection rates and the incidence of tuberculous disease. Students completed the first two medical years with only 8 per cent of non-reactors now becoming

positive. There have been no cases of tuberculosis among the students of two classes which have been followed through to graduation subsequent to the revision of practices in the pathology course.

Meade's experience relating to the development of tuberculous disease among students entering medical school as non-reactors is of special interest. Among 138 students who were reactors at entrance, there were four, 2.89 per cent, who developed tuberculosis before graduation. Of 175 students negative on entry who became positive during training, there were 27 cases of tuberculosis, 15.4 per cent of the group. In this series of cases the average interval between the first known positive test and the detection of a pulmonary lesion was 7.6 months. This experience is in keeping with that of other investigators.

Morris,[5] reporting on the observation of 449 women medical students over a period of twelve years, sums up her experience as follows: "An infection rate of 100 per cent, x-ray evidence in 16.7 per cent, a clinical morbidity rate of 12.5 per cent, a case fatality rate of 10.7 per cent and a mortality rate of 1.3 per cent developing in a stronghold of medicine with facilities readily available certainly constitutes a challenge of sufficient magnitude to interest the entire medical profession in a survey of conditions in other medical educational institutions and hospitals." Morris observed the time relation of tuberculin conversion and the subsequent development of pulmonary lesions in a group of 38 students. In 22 of these there was x-ray evidence of disease within six months of the conversion date and in 12 others the interval was under one year. Israel[7] and his co-workers report that 12.3 per cent of nurses who were non-reactors at the beginning of training developed clinical tuberculosis as compared with 9.4 per cent developing lesions among those originally reactors. They call attention, also, to the earlier development of disease among non-reactors. They state: "The time occurrence of tuberculosis differed distinctly in students tuberculin negative on admission and those who were tuberculin positive. In the former group the lesions developed considerably earlier and the attack rate fell off sharply during the third year. Among students reacting to tuberculin on admission the attack rate rose very slowly and reached its maximum in the third year of training." Zacks and Sartwell[12] studied the inmates of an institution for the feebleminded and found a higher incidence of tuberculosis among non-reactors. This they attributed to conditions which favored heavy exposure, as indicated by high infection rates. Their comment on this phase of the problem is as follows: "One may expect that, in persons whose environmental contact with tuberculosis is heavy and con-

tinuous, most of the cases will develop among non-reactors." Similar findings are reported by Heimbeck and others in numerous publications from Oslo, Norway, dealing with medical students and nurses who have spent considerable periods of training on various tuberculosis services. The foregoing reports seem, therefore, to present a rather definite pattern. This may be summed up as follows: An environment which provides for repeated, and at times, heavy dosage of infection with tubercle bacilli invariably contributes to high infection rates among young adults. If such exposure extends over a considerable period of time, reinfection may follow closely upon a primary infection which has produced a high degree of hypersensitivity to tuberculoprotein. Under these conditions, pulmonary lesions of the reinfection type frequently develop within relatively short periods following primary infection. The size of the dose of tubercle bacilli undoubtedly plays a major role in the production of such a picture. This is emphasized by Rich and McCordock.[13] Commenting on the role of immunity and allergy in tuberculosis they say: "Tubercle bacilli introduced into the body of an infected animal appear to be held locally, i.e., to spread less rapidly from the site at which they first lodge and furthermore, they are undoubtedly less able to survive than they are in the tissues of a normal animal. The infected body becomes changed in some manner which renders the bland protein of the tubercle bacillus capable of acting upon the tissues as a powerful irritant or poison. As a result of the change, the cells of the allergic body are more extensively damaged and killed by a given amount of tuberculoprotein than are the cells of the normal body. More extensive damage and death of cells and more extensive, acute inflammation, constitute, therefore, the local, visible expression of the action of allergy."

In our observation of medical students during the past fifteen years the appearance of a parenchymal lesion of the reinfection type following closely upon primary infection has been encountered but rarely. In only one student has this interval been under one year. Moreover, a higher percentage of our students who entered as reactors have developed pulmonary lesions of the reinfection type than those entering as non-reactors. Gerberding[14] has reported similar findings in his observation of primary infection in young adults in Germany. He states: "The morbidity of those who have a negative tuberculin test is lower in Germany than in the more northerly located European countries." He is not in accord with those who claim that a high degree of protective immunity is conferred by primary infection. "Although it is no longer generally accepted that the healed primary tuberculous focus causes a specific immunity, the author is inclined to believe

that the healed primary focus provides some protection against small, occasional new infections and, on the other hand, is maintained and renewed by such infections." Myers[15] and his co-workers carefully observed the results of primary infection in a group of 423 student nurses and 134 medical students. Of this entire group of 557 young adults, all of whom became reactors to tuberculin while under close supervision, only three developed early spmytoms which might be attributed to tuberculosis. All three developed erythema nodosum. Twenty six students showed x-ray shadows which were interpreted as representing the parenchymal involvement due to primary infection. Regarding their experience as to the significance of primary infection acquired in young adult life, they comment as follows: "The primary complex as it develops in the body of the adult is a benign disease and apparently is of no more clinical significance than the complex which develops in the body of the child." Our experience with relation to primary infection acquired by medical students has been quite similar to that reported by Myers. Four students developed pulmonary lesions which we considered to be of the primary infection type. These were small, sharply delimited areas of a nodular type of density which made their appearance at about six to eight months after the development of sensitivity to tuberculin. In our experience, these have a tendency to persist over long periods of time and do not clear as readily as the exudative type lesion of reinfection. Since there is danger of breakdown and spread from these primary pulmonary foci they should be kept under closest scrutiny including frequent chest roentgenograms. The picture presented by primary tuberculous infection in adults differs in several important respects from that so frequently seen in infants and children. Pulmonary involvement is apparently much less frequent in the adult, the parenchymal lesion is more frequently localized in the upper portions of the lung and is practically never encountered as the massive, pneumonic type of process so characteristic in early childhood. We have followed several hundred students for periods up to several years following primary infection, with chest films at rather frequent intervals, and we have never seen the pronounced hilar node enlargement proceeding on to calcification which is so common in infants and young children.

The specificity of the tuberculin test has been well established although very few studies have been conducted with results that would indicate any real significance on a quantitative basis. However we have observed a small number of students in whom markedly increased sensitivity to tuberculin was followed in a few months by the development of significant pulmonary lesions. Some of our students are rather apprehensive about the dangers

of contracting tuberculosis and come to us as often as every two or three months for retesting with tuberculin and chest x-rays. We have, therefore, had the opportunity to retest frequently students who were slightly sensitive only to the larger doses of tuberculin. The following case history is one of several such experiences which have been of particular interest. A student had normal chest films in his first and second years during which time he was negative to the usual first test dose of 0.01 mg. old tuberculin, but gave a one plus reaction to the second dose of 1.0 mg. old tuberculin. At the beginning of his third year he had two courses, one following the other, in which he stated there was definite contact with advanced, open cases of tuberculosis. On October 5, 1936 he was again negative to 0.1 mg. and slightly positive to 1.0 mg. of old tuberculin. Chest x-ray inspection on November 13 was again negative. On November 21 he reported for another tuberculin test because of his continuing exposure to tuberculosis. The 0.01 mg. dose of old tuberculin now produced a strong three plus reaction. It was recommended that he have chest x-ray at intervals of six to eight weeks. He did not return, however, until April 6. At this time x-ray revealed a small, left apical lesion and tubercle bacilli were demonstrated in the sputum two weeks later. We are now following rather closely a considerable number of students who react only to the larger dose of tuberculin. By frequent testing, we hope to determine what proportion of students may exhibit a marked increase in sensitivity, especially following known exposure to tuberculosis. Frequent x-rays of those showing this change should throw considerable light on its significance in the subsequent development of tuberculous disease.

SUMMARY

Programs for the control of tuberculosis among college students are now being conducted at several hundred institutions. The incidence of tuberculous infection among entering students has shown a very significant decrease during the past fifteen years. In most sections of the United States less than 30 per cent of undergraduate students react to tuberculin and in many areas, less than 20 per cent.

During the past fifteen years a continuous program of tuberculosis case finding at the University of Pennsylvania has resulted in the detection of 177 students with pulmonary tuberculosis. Medical students and nurses frequently show surprisingly high rates of infection during their training, a condition which invariably gives rise to a high incidence of disease. Tuberculin tests applied at intervals of two months provide a most accurate method of determining those phases of medical school training

which offer the greater risks of tuberculous infection. Chest roentgenograms should be provided for all medical students who are reactors to tuberculin at least twice during each academic year.

RESUMEN

Actualmente varios cientos de instituciones cuentan con programas para el control de la tuberculosis entre los estudiantes de colegio. La frecuencia de la infección tuberculosa entre los nuevos estudiantes ha mostrado una disminución muy significativa durante los últimos quince años. En la mayoría de las secciones de los Estados Unidos menos del 30 por ciento de los estudiantes aún no graduados reaccionan a la tuberculina y en muchas zonas, menos del 20 por ciento.

Durante los últimos quince años un programa contínuo para el descubrimiento de casos de tuberculosis en la Universidad de Pennsylvania ha resultado en el descubrimiento de 177 estudiantes con tuberculosis pulmonar. Los estudiantes de medicina y las enfermeras frecuentemente presentan durante su adiestramiento índices de infección sorprendentemente elevados, lo que invariablemente produce un alto porcentaje de enfermedad.

REFERENCES

1 Long, Esmond R.: "Tuberculosis in College Students with Special Reference to Tuberculin Testing," *Jour. Lancet*, 55:201, 1935.
2 Furcolow, M. L., Hewell, B., Nelson, Waldo E. and Palmer, Carrol E.: "Quantitative Studies of the Tuberculin Reaction," *Public Health Reports*, 56:1082, 1941.
3 Long, Esmond R.: "The Tuberculin Test," *Am. Rev. Tuberc.*, 40:607, 1939.
4 Soper, Willard B. and Amberson, J. Burns: "Pulmonary Tuberculosis in Young Adults," *Am. Rev. Tuberc.*, 39:9, 1939.
5 Morris, Sarah I.: "Tuberculosis as an Occupational Hazard During Medical Training," *Am. Rev. Tuberc.*, 54:140, 1946.
6 Boynton, Ruth: "The Incidence of Tuberculous Infection in Student Nurses," *Am. Rev. Tuberc.*, 39:671, 1939.
7 Israel, Harold I., Hetherington, H. W. and Ord, John G.: "A Study of Tuberculosis Among Students of Nursing," *J.A.M.A.*, 117:839, 1941.
8 Riggins, H. M. and Amberson, J. Burns: "Detection and Control of Tuberculosis Among Nurses," *Am. Jour. Nursing*, 40:1137, 1940.
9 Brean, Henry P. and Kane, Lewis W.: "Pulmonary Tuberculosis in Harvard Medical Students," *New Eng. Jour. Med.*, 235:10, 1946.
10 Hedvall, Erik: "The Incidence of Tuberculosis Among Students at Lund University," *Am. Rev. Tuberc.*, 41:770, 1940.
11 Meade, Gordon: Presented before the Am. Trudeau Society, Eastern Section, New York, Nov. 8, 1946.
12 Zacks, David and Sartwell, Philip E.: "The Development of Tuberculosis and Changes in Sensitivity to Tuberculin in an Institution for the Feeble-minded," *Am. Jour. Pub. Health*, 32:732, 1942.
13 Rich, Arnold R. and McCordock, Howard A.: "Roll of Allergy in Tuberculosis," *Bull. Johns Hopkins Hosp.*, (May), 1929.
14 Gerberding, H.: "The Problem of Tuberculous Infection in Young Adults," *Zeitschrift für Tuberk.*, Leipzig, 85:101, 1940.
15 Myers, J. A., Ch'Iu, Philip T. Y. and Streukens, T. L.: "Primary Infection in Adults," *Am. Rev. Tuberc.*, 39:232, 1939.

The Place of Psychiatry in the Program of a Tuberculosis Hospital*

ALLAN HURST, M.D., F.C.C.P.,** JULES V. COLEMAN, M.D.**
and RUTH HORNBEIN, M.S.S.**
Denver, Colorado

Tuberculosis is an illness in which the scale of emotional involvement is of particular interest. Disturbance of feeling is promptly and deeply aroused. The response of the patient is partly the reflected shadow of social myth and superstition; it is partly an awareness of the personal and social implications of the illness itself; and partly it represents an emergence of latent, specifically individual infantile and neurotic potentialities.

By its very nature, the illness imposes upon the patient the threat of violation of the integrity of his personality, and changes the meaning and direction of his life course. It is a crippling illness in a real sense, since there is so high an incidence among people in the productive years of life. The social stigmatization associated with tuberculosis places the patient in an outcast situation, and the nature of hospital treatment, with its enforced inactivity and dependency, engenders feelings of parasitism and uselessness. Again, where surgical procedures are carried out, feelings of mutilation, of damage to the body image, are common and highly disturbing. In each phase of the illness, there are special reactions of anxiety which present important problems of management and care.

The psychiatric program at National Jewish Hospital, in its steady expansion, has revealed a growing awareness of the major importance of psychological factors in the onset, course, and outcome of tuberculosis. Initiated in 1936 by Dr. Charles J. Kaufman, the previous medical director, it has demonstrated that psychological understanding and management are indispensable in the care of the tuberculous patient.

In previous papers, we have discussed some of the psychological problems encountered in the tuberculous patient. In this paper, we shall review the problem of the administrative integration of psychiatric service in a tuberculosis hospital, from the standpoint of certain general principles in applied psychiatry, as well as

*Presented at the 14th Annual Meeting, American College of Chest Physicians, Chicago, Illinois, June 20, 1948.

**From the National Jewish Hospital and the Mental Hygiene Clinic of the University of Colorado Medical Center, Denver, Colorado.

the specific ways in which psychiatric time is used in relation to these principles.

The first general consideration is that the patient in the hospital finds himself in a situation of group living with relations to the staff which are defined by hospital rules and routines, and by the psychological nature of medical authority. As a result, the role of the patient resembles the dependent situation of the child, and the staff role the position of the parent in a family group.

An important aspect of this staff-patient relationship is its ambivalent character. The patient's dependence on the staff for the gratification of his needs for affection and care makes him particularly vulnerable to feelings of frustration and resentment. The expression of such feelings often leads to patients being described as uncooperative and to their discharge as disciplinary problems. The hostility of the patient is thus met not with an effort at an understanding of its origin, but with counter-hostility from the hospital authorities.

A hospital psychiatric service may be oriented to direct work with the patients, and may then be described as "patient-centered," or it may be oriented to the task of helping the people who carry the actual day-by-day responsibility for the patient, and this then is a "staff-centered" psychiatric service.

Our experience has been that a "patient-centered" psychiatric program in a tuberculosis hospital tends to be sterile, unproductive, and unrewarding. It has little or no value as a technique of staff development in comprehensive patient care; it makes no contribution to the problem of the hospital management of the patient; it leaves to one side the possibility of bringing into being a psychologically-enriched view of the illness, and of the experience of the patient with his illness and its treatment.

The attitudes, prejudices, intolerances, and personal problems of the hospital staff are as much a part of the patient's experience with his illness as what goes on in his chest, or for that matter, what goes on in his personality. If medical care is not correlated with consideration for the social and psychological situation of the patient, it reduces itself to technical absorption and tends to lose the dignity of a professional character. Psychiatric care may fall into the same pitfall of technical isolation.

Most psychiatric programs in tuberculosis hospitals begin on a "patient-centered" basis. The service is offered to individual patients or to groups of patients, with attention focused on intrapsychic process, very often without consideration of its relation to hospital living. Most psychiatric problems in the tuberculosis hospital do not require specialized psychiatric treatment but may be handled through the understanding and proper orientation

of the staff. On the other hand, a "staff-centered" program does not exclude direct treatment of the patient by the psychiatrist in the small percentage of cases where it is indicated.

We have found that, given the opportunity, members of the staff are eager to discuss the problems they have with patients, are eager to enlarge their own understanding, and are able to find comfort, reassurance, and help through discussions with the psychiatrist or the psychiatrically oriented social worker which meet them at their own level of thinking and feeling.

In the hierarchy of staff members as parental figures, the physician occupies a special role because of his key responsibility for the medical destiny of the patient. Actually patients are always bringing or wanting to bring their personal problems to the attention of the physician. There are many doctors who are talented in the intuitive grasp of the personal problems of their patients, and deal with them understandingly and successfully. Because of the special nature of the doctor-patient relationship, the patient may often be able to confide more directly and more intimately to the doctor who is responsible for medical management than to any other person, including the psychiatrist.

However, it is misguided, and even somewhat naive to expect a physician who is untrained in psychiatry to be able to understand the personality structure of the patient, the dynamics of his reaction to his illness, his medical care, and his hospital experience, or the interplay of personality in the staff-patient relationship as it affects the patient's response. While we have found considerable variation in psychological flair and capacity among our staff physicians, there is little doubt that the opportunity to share in the psychiatrist's thinking and to make use of the psychiatrist's time for consultation on cases is of great value.

Certainly the physician without thorough psychiatric training and particularly without extensive training in the dicipline of psychotherapy runs the risk of allowing the patient to develop unconscious, intense emotional reactions which must be handled to avoid psychological damage. These are reactions such as acute episodes of hostile, irritable, spiteful behavior, or completely submissive attitudes of devotion and love, like the "crushes" of the adolescent, sensitizing the patient to every gesture and imagined whim of the doctor. These reactions are the result of retained infantile impulses, which are generally kept under cover but which may break through in any intensive doctor-patient relationship. As a result of his training, the psychiatrist is able to recognize these manifestations, and to make use of techniques which will either keep them under control or allow them to be dealt with skillfully as they appear.

We see the role of the psychiatrist, then, as that of participant in the common effort of general care of the patient, as a member of the clinical team of the hospital, in which each professional group, including the physician, nurse, social worker, psychologist, occupational therapist and vocational adviser, contribute from their own professional training and experience, and by the use of their own professional methods, to the welfare of the patient.

From the point of view of the psychiatrist, the contribution of the psychiatrically oriented social worker is particularly important. In addition to rendering direct social and personal services, the social case worker is in a position to offer the patient a unique continuity of interest in relation to such problems as his separation from family, adjustment to hospital routines, family needs, and preparation for re-establishment in the community. Furthermore, the social worker has received extensive instruction during her school experience in modern, dynamic, psychiatric concepts, and has, at this point, more training than the physician in the observation and understanding of personality processes. Psychiatric services can therefore be most effectively deployed in terms of the concept of participant psychiatry in hospital settings where psychiatrically oriented social service is soundly developed.

From the vantage point of this general introduction, we shall now discuss the specific ways in which psychiatric services are employed at the National Jewish Hospital. There are four main types of activity, including consultation, teaching, treatment, and research. These activities are all inter-related and interdependent, and all represent important elements in a program of psychiatric services in a tuberculosis hospital.

Consultation: In many ways, this is the most basic contribution of the psychiatrist. The two main groups to whom such consultation is available are the physicians and the social workers, and these are the staff persons who deal most directly with the personal problems of patients. The psychiatrist may interview the patient and then discuss the case with the interested staff member, or more commonly, the discussion is on the basis of case material presented by the doctor or worker. Since the emphasis is on helping the staff person in his problems with the patient, recognition must be given to the person's own way of dealing with interpersonal problems, the extent of his understanding, his limitations in understanding, his own feelings about the patient's behavior, i.e., what it means to him; whether he is over-identifying with the patient's problems, or rejecting the patient and unable to accept the problems. These are all considerations which influence the psychiatrist's activity, and it will be of interest to the psychiatrist to explore how far the staff person can go in recognizing

his own role in the relationship, to what extent he can be helped with prejudicial attitudes, and most important, to attempt to relieve anxieties which he has developed in his dealings with the patient.

Teaching: Although consultation is the core of the psychiatric service, a program of education in psychiatric thinking is carried out through seminars and group discussions, with the object of procuring acceptance from the staff of certain basic principles, for example, (1) that behavior is always meaningful, motivated, and dynamic, i.e., a product of interaction of personality forces; (2) that there is an intimate relationship between the patient's emotional life and what happens to his disease; (3) that the interests of comprehensive medical care require that proper consideration be given to the patient's personal problems and his emotional difficulties; and (4) that the patient's experience in the hospital, in his relations to staff, is important to the course of his illness.

Psychosomatic seminars are held regularly, and are attended by all members of the professional staff. In addition, courses in psychosomatic problems are given to student and graduate nurses and to occupational therapists by the chief social worker.

In passing, it might be mentioned that an educational program is also carried out for patients. Its purpose is to orient patients at every phase and in every respect of their disease and its management, including consideration of emotional attitudes and problems; its productive results are described in another paper.

Treatment: Our general policy has been to offer direct psychotherapy to any patient who expresses an interest in such treatment. The actual number of patients in psychotherapy is probably greater than at most tuberculosis hospitals, since many patients are referred for the purpose of receiving direct psychiatric treatment, as well as for the care of their tuberculosis. At the present time, there are about twenty patients in psychotherapy. There are some who are being treated by the consulting psychiatrists in connection with the research project, some are seen by the staff psychiatrist, and others are treated by psychiatrists from the Mental Hygiene Clinic of the University of Colorado Medical Center.

A special aspect of psychotherapy is that of helping the patient to adjust to his hospitalization. A number of patients are admitted with marked evidence of reactive anxiety, expressing fear for their future, fears about their family and fears about surgery. There is often marked relief of anxiety after a few psychiatric interviews. We have found that a good deal of this work could be done by social workers under the supervision of the psychiatrist.

In some instances, for example, in four cases of homosexuality being seen by the staff psychiatrist at this time, the training and skill of the psychiatrist are needed to help the patient to accept the limitations imposed by hospitalization and to learn to live with his psychiatric problem during the period of treatment.

Problems which require particular understanding are those in which the patient displays marked responses of hostility, dependence, and anxiety. Very many instances of aggressive, defiant, resistive, and negativistic behavior may become acceptable and manageable when understood in terms of these basic responses, which are in constant interaction with one another. Anxiety, for example, may lead to an increased need for evidences of interest and affection from the staff, or to feelings of frustration, with mounting irritability and aggressiveness.

The very situation of dependence which is inherent in being hospitalized creates anxiety in some patients. Others have always had difficulty in accepting authority, and react to routinized and restricted living with hostile feelings, which in turn may produce anxiousness and fears of rejection.

The patient who is constantly seen out of bed, who seems to delight in a display of butt-filled ashtrays, who seems to swagger in an attitude of challenge, may be reacting to feelings of insecurity, testing the physician to gain reassurance that he is accepted anyway, seeking love and care through his devious and painful distortions of behavior. Similar behavior may be found in other patients whose feelings of tension and reservoirs of guilt can only be relieved by provoking criticism and punishment from the staff.

These few examples illustrate the importance of obtaining a clear and full picture of the personality of the patient presenting emotional or behavioral problems. They add weight to our premise that understanding of personality factors is often essential in formulating a comprehensive program of medical care for the patient.

While direct psychiatric treatment has a real place in the tuberculosis hospital, it is also important to stress the need for individualized understanding of all patients, and for psychotherapeutic orientation of the hospital program as a whole. From this point of view, routines and regulations, policies and procedures should be constantly re-examined and reviewed, and subjected to revisions which seem necessary in the interest of protecting the emotional situation of the patient.

Research: A continuous process of enquiry into the relations between tuberculosis and emotional reaction is as essential in the maintenance of high professional standards as is research

in the biological and clinical aspects of tuberculosis. For the past year, a pilot study in psychosomatic inter-relations in tuberculosis has been under way. We have tentatively concluded that there are no specific trends or patterns of emotional disturbance to be found in the patient with pulmonary tuberculosis but that a statistically significant percentage were in states of emotional upset in relation to current life situations in the period preceding the physical breakdown. There is also some evidence of a positive correlation, as in essential hypertension, between the status of hostility in patients and the course of their illness.

SUMMARY

We would emphasize that all of the aspects of psychiatric service which we have outlined above are important, and need to be effectively integrated in the development of a sound program of psychiatry in a tuberculosis hospital. For example, we would regard it as a forlorn hope to attempt to carry out a limited teaching program in the psychiatric aspects of tuberculosis, and expect that it could then be applied without the continued participation of a psychiatrist and psychiatrically oriented social worker.

We therefore stress the need for continuity of a program as we have outlined it, and also the need to orient such a program on the basis of a concept of participant psychiatry.

Discussion

WILLIAM C. VOORSANGER, M.D., F.C.C.P.
San Francisco, California

You have heard a very interesting paper on the relationship between tuberculosis and psychiatry in a big hospital. I shall discuss the subject from the general aspect of all patients with tuberculosis, those who are cured and those who are not, and the approach necessary to keep them happy and satisfied. I have stressed for years, in lectures to doctors, students and nurses, that tuberculosis is a three-fold entity; primarily a pathology; next a sociology; and third, a psychology.

I might cite a case with an interesting psychologic slant. This woman was in a sanitorium—not as large as the National Jewish, but it had 60 beds and a considerable number of patients. Her husband said to me one day that he had attended one of Aimee McPherson's sessions, had seen her cure a child of deafness and wanted to take his wife to see her. I presume you all remember Aimee—she was an evangelist who worked entirely on personality.

I said: "Your wife is getting along very well; has she no faith in me?" He said: "She has perfect faith in you." I said: "What can Aimee McPherson do that I cannot do? I have as much education as she, and more. I have medical training which she has not." He said: "Yes, but she cures through faith in Jesus Christ." I said: "Well, why can't I do that?" and he said: "You know I never thought of that!"

The treatment of the family of a patient with tuberculosis and the solving of their problems is just as important as treating the patient. When a man has tuberculosis and a wife and four children at home, and no money to feed them, I can't see that psychiatry and psychology will do any good. That man needs a few real dollars to take care of his family, therefore the approach is not to try to cure the man's emotional state but to see that somebody supplies food for the family. Another angle is one in which there may be no economic problem; where a man is doing fairly well and his wife and daughter come to see him three times a week and stand at the bedside and cry. There is no use telling that man not to be emotional; the thing to do is tell his family not to be emotional.

There are numerous angles. A young man, let us say, 34 years old, married, has had tuberculosis for fourteen years, undergone a four-stage thoracoplasty and still is not well. I would feel emotional under those circumstances. How can we explain to that patient that the future holds some promise for him? I don't believe any psychiatrist can handle that. Or consider the case of a woman who gets well, whose husband is so afraid that she will infect his children that he makes her live apart from the family. It isn't the patient who needs treatment; it is the family who must be given the understanding that the patient is now well and will not infect the children. There are certain nationalities, Italians and Greeks and Portuguese, upstanding people in the community, who still have this awful fear of contagion. Then there is the angle where the patient is constantly fearful that he or she will infect the children. Those are real problems that we, as doctors, not as psychiatrists, must face.

I do not believe it takes a psychiatrist to understand these patients. I believe the prime object of psychiatry, which I recognize as a great science, whether in a hospital or outside, should be to train doctors and social workers to understand how to approach the emotional problems of these patients. I recognize that in tuberculosis as in all chronic diseases there may be neuroses, there may be psychoses, there may be psychosomatic conditions. There may be times when you must call the psychiatrist into consultation, but I believe his main job to be to teach the doctor

who is treating tuberculosis that, in addition to the pathologic aspect, there are sociologic and psychologic aspects; that there are problems in the family as well as in the patient, and that he must strive to understand the personality of the patient and handle him accordingly.

FRANZ ALEXANDER, M.D.

Chicago, Illinois

The contribution of psychiatry to the problem of tuberculosis is a chapter of psychosomatic medicine still to be written. There are two aspects to the problem—the question of etiology and the question of treatment. The emotional state of the patient can be considered in every disease as one of the etiologic factors, because chronic emotional stress has an influence upon all vegetative processes and does alter the resistance of the whole organism or of specific organs.

In the 19th century tuberculosis was the literary disease. The discovery of the bacillus of tuberculosis by Koch did not in the least invalidate the observation of earlier literary and medical men, that the outbreak of the disease often follows catastrophic events in the patient's life. Unfortunately, we do not know today much more than did these earlier observers about the specific nature of the traumatic emotional factors in tuberculosis.

Apart from precipitation of the disease, its course may be influenced by emotional factors. The resistance of the organism definitely depends upon the emotional state. Exactly how emotional processes increase or decrease the resistance of certain tissues we do not know. That is one of the most challenging problems for future research, and its solution may revolutionize therapy as much as have recent pharmacologic discoveries. Today our knowledge is merely empiric. We know that attention to the patient's emotional state is a prerequisite of sound medical care, and that this requires the technical knowledge of psychiatry cannot be contradicted. However, one may hope that with further progress in medical education, in the not too distant future every physician will have sufficient knowledge of the basic principles of psychiatry, so that he may include in his treatment considerations for the proper mental hygiene of his patients. Today the basic principles of bacteriology and physical hygiene belong to the conceptual armamentarium of every well-trained physician. He does not need to consult a bacteriologist to advise his patients in this respect. It can be hoped that in the not too distant future hospitals will use their psychiatrists only for treatment of special

cases, and will be able to entrust routine mental care of patients to the staff as a whole.

Such every day, typical psychiatric problems as have been pointed out in this paper, the tendency for hospitalized patients suffering from chronic diseases to regress to a state of excessive dependency, manifesting itself in an irritating, demanding attitude, will have to become for every physician a matter of routine, just as are today bedsores or other common somatic sequelae of prolonged bed rest. The program of the National Jewish Hospital at Denver certainly is setting an exemplary standard for others to follow. In addition to the reform of undergraduate training, this type of consultation and teaching programs in hospitals can become important factors toward consolidating the new psychosomatic orientation which characterizes our present medical development.

RESUMEN

Querríamos recalcar que todos los aspectos del servicio psiquiátrico que hemos bosquejado en este artículo son importantes y deben ser integrados efectivamente en el desarrollo de un adecuado programa de psiquiatría en el hospital para tuberculosos. Por ejemplo, nos parecería ser una empresa desesperada el intentar llevar a cabo un programa de enseñanza limitado en los aspectos psiquiátricos de la tuberculosis y esperar que podría ser aplicado sin la contínua participación de un psiquiatrista y de un auxiliador social con orientación psiquiátrica.

Por consiguiente, recalcamos la necesidad de continuar el programa que hemos bosquejado y de orientar tal programa a base del concepto de participación psiquiátrica.

Thoraco-Hepatic Amebiasis*

MICHAEL F. KOSZALKA, M.D., FORRESTER RAINE, M.D.
JAMES P. CONWAY, M.D. and MISCHA J. LUSTOK, M.D., F.C.C.P.
Wood, Wisconsin

World War II has created and brought into closer focus many, heretofore remote, clinical problems. One of these is amebic infection.

The mass concentration of military personnel into areas endemic to amebiasis and the exposure of the soldier to a terrain devoid of sanitary control prior to his arrival, contributed appreciably to the epidemiology of this disease. Sanitary regulations, especially if made purposely severe to compensate for lack of sanitary installations, are often disregarded under stress of combat areas.

It is documentary knowledge[1] that one regiment, (under observation of J.P.C.), left an endemic area with a carrier rate of 23.4 per cent—as determined by rectal swab and normal stool examinations. If fresh warm stools passed after a saline purge were examined, no doubt the percentage would have been even higher. This figure is unusually high for Americans, and cannot be construed as an index of the carrier rate of all returned servicemen, but should focus the attention of the physician to a plausible etiology for the vague gastro-intestinal and pulmonary complaints of many veterans who have served in the Pacific Theater. Service in the tropics is not, however, an essential prerequisite for such a diagnosis, for similar opportunities for amebic infestation existed within the endemic areas of the Zone of the Interior.

We were interested in a group of patients with amebic infestation whose major presenting symptoms were of a pulmonary nature and whose early presenting signs were conspicuous in the thorax. History of diarrhea was lacking or of mild nature. Little significance had been attributed to it by the patient or the physician. Frequently the patient was seen by the chest consultant first, because of the emphasis placed on the thoracic signs and symptoms. Only after intensive etiological study at first, and more readily after experience matured, was the true secondary nature of the chest lesions fully appreciated and proper definitive

*From the Medical and Surgical Services, Veterans Administration Hospital, Wood, Wisconsin, and Marquette University School of Medicine. Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinion expressed or conclusions drawn by the authors.

management instituted. Classical signs of amebic infestation or typical medical history often were absent or vague in our cases. The type of patient who presents an adequate history, would have been screened and definitely managed in his earlier contacts with physicians.

The recovery of the parasite from the stool or tissue studies is the ideal criterion for diagnosis. This is difficult in some cases. In our experience, the presence of acute or recurrent right lower chest findings (effusion, pneumonitis, lung abscess) in an individual who lived in endemic areas, especially if associated with evidence of chronic hepatic involvement, has been adequate presumptive evidence for the clinical diagnosis of thoraco-hepatic amebiasis and indication for proper therapeutic procedures.

Case Reports

During 1946, we had the opportunity to observe and treat ten patients with thoraco-hepatic amebiasis. Two patients had uncomplicated hepatitis; two had hepatic abscesses, one of which ruptured into the abdominal cavity; in three, a hepatic abscess had ruptured into the pleural cavity, one of which had also ruptured into the abdominal cavity; and in three, the hepatic abscess had entered the pulmonary parenchyma. Six had served in the Armed Forces in the Southwest Pacific; one in the India-Burma Theater, and three had never left the continental United States.

It is interesting to note that only four of these ten patients

FIGURE 1

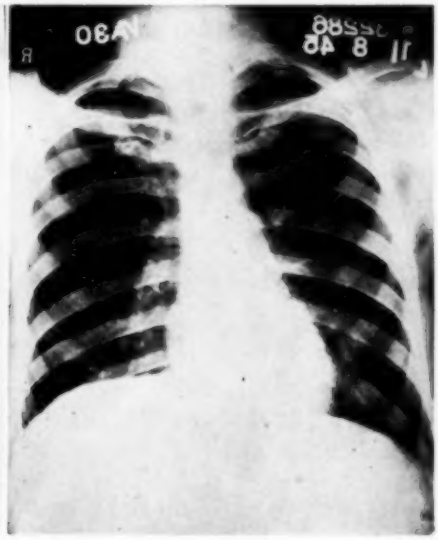


FIGURE 2

Fig. 1, Case 1: Intra-hepatic density of liver abscess.
Fig. 2, Case 1: No significant chest involvement.

gave a history of diarrhea, and then not as a major event. Eight presented pulmonary and thoracic signs and symptoms of primary significance. Cysts of E. histolytica were recovered on stool examination in only four of this group. A direct smear from the wall of a liver abscess in one of the patients at postmortem examination contained the amebic trophozoite.

Case 1: N. A., 35 year old male, Army veteran, served in the Southwest Pacific in 1943 where he contracted malaria. He had six to nine recurrences. He was treated for malaria for two weeks prior to admission because of chills, fever and headache. Soreness in the epigastrium and bilateral costal margins and later vomiting appeared. A weight loss of 38 pounds was reported. No past history of diarrhea or dysentery was elicited. On admission, October 13, 1945, he appeared chronically ill. He was jaundiced and was tender in the epigastrium. He developed pain and tenderness in the right upper quadrant which spread to right lower chest. The liver became enlarged and tender. He ran an irregular, intermittent fever. A laparotomy done on November 10, 1945 revealed an abscess, 12 x 17 cm. in diameter in the upper posterior portion of the liver. There was a smaller one on the inferior surface. They contained thick, chocolate-colored pus. The abscesses were incised and drained and the patient was placed on emetine therapy postoperatively. The abdominal operative wound drained profusely. After showing some improvement, he ran a septic downward course and expired December 27, 1945. Necropsy confirmed the postoperative diagnosis by demonstration of E. histolytica on direct smear from the wall of the liver abscess (Figs. 1 and 2).

Case 2: E. S., 22 year old male, Army veteran, who served for approximately one year on Luzon and New Guinea in 1944-45, was admitted to

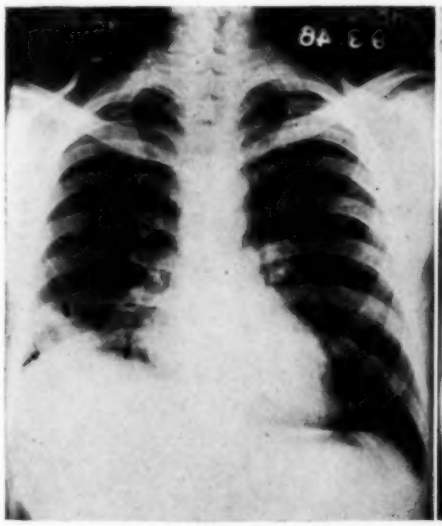


FIGURE 3

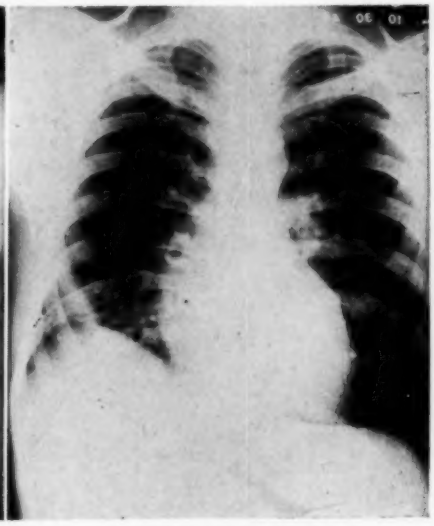


FIGURE 4

Fig. 3, Case 2: Extension of hepatic amebic abscess into pulmonary parenchyma.—*Fig. 4, Case 2:* Fibrotic residuals after spontaneous bronchial evacuation of lung abscess.

the hospital August 21, 1946, complaining of diarrhea of six month's duration. He had six to ten bowel movements daily containing blood and mucus. He had no diarrhea or dysentery overseas. Three weeks prior to hospitalization, he noticed the onset of aching pain in the right lower chest and right upper abdominal quadrant. At the same time, he developed a cough and pain in the right shoulder. Increasing weakness and exertional dyspnea occurred. Physical examination showed a pale, asthenic, chronically-ill white male who had a fever of 102 degrees F. There was limitation of expansion of the right chest with diminished breath sounds and tactile fremitus, as well as an impaired percussion note in the right lower lung field. There was tenderness in the epigastrium. Stools were positive for trophozoites of E. histolytica. He began expectorating chocolate-colored pus on August 26. The diarrhea subsided completely and his temperature came down to normal after a course of emetine therapy followed by carbarsone. Proctoscopic examination on August 29 showed small pin-point bleeding ulcerations suggestive of amebic colitis. A course of emetine and carbarsone was repeated beginning on October 14. Sixty cubic centímeters of chocolate-colored fluid were aspirated from right chest on October 18. No organisms or parasites were demonstrable in the fluid. The patient was clinically well by November 9, 1946. Surgery was held in abeyance because of excellent clinical response to medical management (Figs. 3 and 4).

Case 3: A. B., 27 year old male, Army veteran, entered the hospital on July 15, 1946. He had diarrhea in the Philippines and Okinawa in 1945. An initial diagnosis of amebic dysentery was made at Oakland Regional Hospital. While there in January 1946, the patient began coughing up foul-smelling sputum which tasted like "pine-cone seeds." Following a course of emetine, he recovered and was discharged as well in March

FIGURE 5

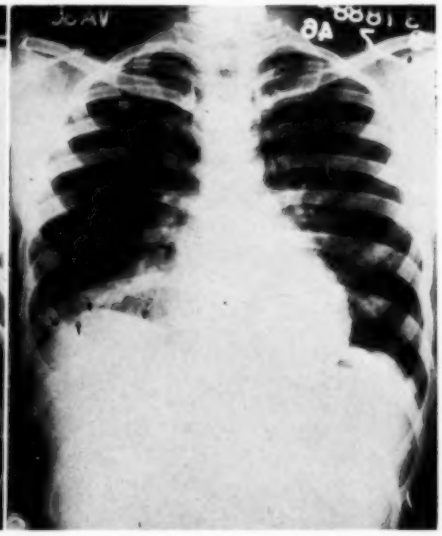


FIGURE 6

Fig. 5, Case 3: Rupture of hepatic abscess into lung parenchyma.—*Fig. 6, Case 3:* Spontaneous evacuation of lung abscess with residual air seen under right diaphragm. This was evidence of broncho-hepatic fistula and indicated surgical intervention.

1946. When hospitalized here for a routine check-up on August 6, 1946, he developed a temperature of 103 degrees F., with recurrence of blood-tinged sputum which tasted like "pine-cone seeds." He improved with emetine therapy. (Repeated stool examinations for E. histolytica were negative). A third recurrence of rupture of the amebic liver abscess through the right diaphragm into the right lung on September 17 indicated surgical interference, and on September 27, a thoracotomy with decortication of the right lung was done. Following removal of all drains, his postoperative course was uneventful. He was discharged November 16, 1946, clinically well. He returned on February 10, 1947 for follow-up study and was found to be in good health (Figs. 5 and 6).

Case 4: B. S., 38 year old male, Air Force veteran, entered the hospital August 22, 1946, complaining of generalized chest pains, dyspnea and fever with expectoration of bloody sputum. He had a similar occurrence in June 1946, for which he received penicillin, and salicylates without response. A weight loss of 15 pounds during the past few months was reported. No previous history of diarrhea or dysentery was elicited. All his military service was in the continental United States, but he had come in contact with servicemen from the Philippines who had had amebic dysentery, and had used a common swimming pool. Physical examination showed him to be acutely ill, temperature 101 degrees F., with physical signs of fluid in the right chest. A roentgenogram of chest taken before admission revealed suspicious liver abscess with extension into the right lung. On August 23, 500 cc. of serosanguinous fluid were aspirated from the right chest and on August 28, cysts of E. histolytica were found in his stools. The patient was placed on a course of emetine and diodoquin. An exploratory thoracotomy with decortication and drainage of abscess was done on September 13. His postoperative course was uneventful with subsequent complete clinical recovery (Figs. 7, 8 and 9).

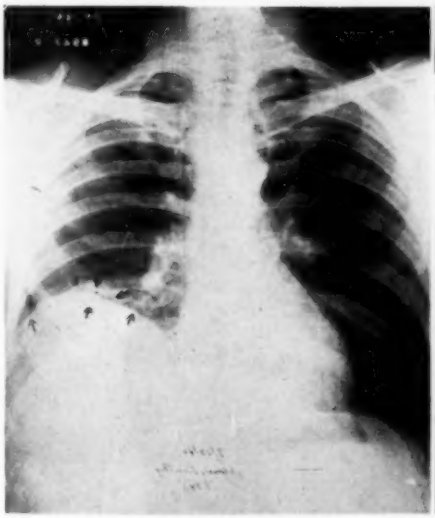


FIGURE 7

FIGURE 8

Fig. 7, Case 4: Liver abscess with linear pulmonary atelectasis above elevated diaphragm.—*Fig. 8, Case 4:* Rupture of liver abscess into thoracic cavity.

Case 5: E. R., was a 24 year old male, Navy veteran, who had served only in continental United States, but came in contact with servicemen who had had amebic dysentery and had used a common swimming pool. He was admitted to the hospital on May 1, 1946, complaining of pain in right chest and cough of three week's duration. The chest examination revealed distant breath sounds and a flat percussion note with crackling rales over right lower and posterior chest. A roentgenogram of the chest revealed a massive effusion in the entire right hemithorax. Aspiration of the fluid revealed a thick, green pus. The underlying lung which became visible after removal of the purulent fluid was suspected of having an intrinsic hepato-pulmonary lesion. All laboratory examinations, including numerous stool examinations, were normal. On May 25, a rib resection with drainage of an empyema cavity 10 cm. in diameter in the right chest was accomplished. A right thoracotomy on July 22 revealed the presence of a subdiaphragmatic abscess which was incised and drained. It contained thick, grayish pus. A revision and broader resection with drainage of the empyema and subdiaphragmatic abscess involving the liver completed the surgery on August 8. Proctoscopic examination was negative. Remittent fever persisted until the patient received a therapeutic course of emetine followed by diodoquin. After several plastic revisions of persistent sinus tracts, complete clinical recovery followed (Figs. 10 and 11).

Case 6: A. M., age 48, was a male veteran of World War I, who served in France in 1918. He had lived in Ohio and Wisconsin all his life. There was no past history of diarrhea or dysentery. He became sick with nausea, pain in the right hypochondrium and fever in July 1944. A laparotomy was done at Veterans Administration Hospital, Brecksville, Ohio, for the treatment of an amebic liver abscess. Drainage was instituted and ultimate recovery of patient resulted. On routine checkup, E. histolytica were found in his stools in January 1945. The patient com-

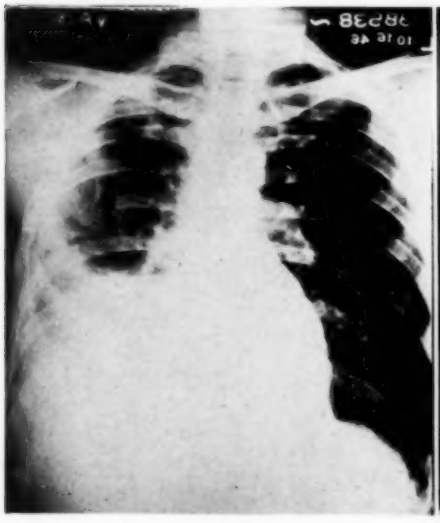


FIGURE 9

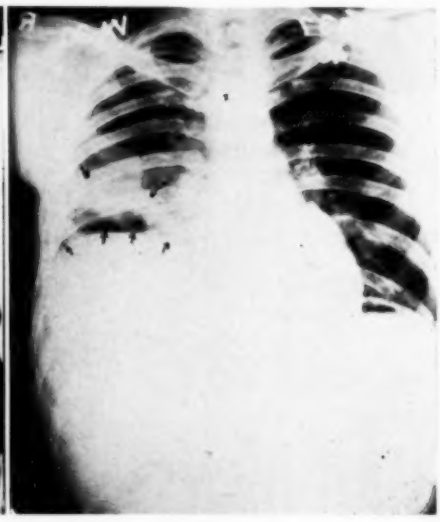


FIGURE 10

Fig. 9, Case 4: Early residuals after surgical drainage of liver abscess and overlying secondary empyema.—*Fig. 10, Case 5:* Elevated diaphragm and overlying encapsulated empyema visible after aspiration of massive right pyothorax.

plained of soreness in the right lower chest and roentgenograms showed elevation of the right hemidiaphragm at that time. His symptoms subsided following a course of emetine. He was admitted to Wood Veterans Hospital on June 17, 1946, complaining of pain in the right lower chest, cough and fever of two week's duration. His stools were positive for cysts of E. histolytica. The patient left against medical advice (Fig. 12).

Case 7: W. J., 26 year old male veteran, entered the hospital on May 9, 1946, complaining of pain in the right lower anterior chest of ten days' duration. The pain became gradually worse and was accompanied by vomiting. A weight loss of 24 pounds in the past six months was reported. He had had amebic dysentery on Leyte in January 1945, which responded to emetine. There have been three recurrences of pain in the right lower chest since that time. No diarrhea was noted with the last two episodes. He showed a respiratory lag, diminished tactile and vocal fremitus, impaired percussion note and diminished breath sounds in the right lower chest. Rigidity and tenderness in the right upper abdominal quadrant was noted. His temperature was 103 degrees F. The stools were negative. His temperature dropped to normal within three days after institution of emetine therapy. He became asymptomatic and the chest findings gradually returned to normal. Surgical intervention was not deemed necessary. Follow-up studies revealed no recurrence of chest disease. This case illustrates probable diagnosis of amebic hepatitis or very early amebic liver abscess with contiguous pleural reaction and effusion (Fig. 13).

Case 8: A. R., a 39 year old male veteran entered the hospital on November 13, 1946, complaining of constant pain in the right upper abdominal quadrant for nine days. Fever, nausea, anorexia and weight loss were noted but no diarrhea was present. He had had diarrhea of seven days' duration while in India in 1944. The physical examination revealed

FIGURE 11

FIGURE 12

Fig. 11, Case 5: Iodized oil visualization of communication between residual empyema cavity and hepatic abscess after surgical drainage.—*Fig. 12, Case 6:* Elevation of right hemidiaphragm with suggestive pointing of a recurrent liver abscess.

a pleural friction rub with diminished breath sounds in the right lower chest. The liver was slightly enlarged and tender. His stools were negative for cysts and trophozoites. The complement fixation test was positive for amebiasis. A therapeutic course of emetine produced complete relief of symptoms and disappearance of physical signs within three days. Therefore, the diagnosis of thoraco-hepatic amebiasis was considered tenable (Fig. 14).

Case 9: R. C., 28 year old male veteran, was admitted to the hospital on July 17, 1946. He had had intermittent diarrhea which started in the Southwest Pacific in 1943. A previous diagnosis of liver abscess had been made in January 1946. He had a temperature of 101.8 degrees F., an enlarged, tender liver and negative chest findings. The proctoscopic examination showed a healed cicatrix on the posterior wall of the sigmoid, interpreted as a healed amebic ulcer. His stools were negative for E. histolytica. A therapeutic trial with emetine produced complete clinical recovery within four days, suggesting the diagnosis of amebiasis.

Case 10: J. A. B., 29 year old male veteran, entered the hospital on January 29, 1946, complaining of fever, weight loss of 30 pounds, pain in the right chest, right upper abdominal quadrant, and malaise. He had been sick for four weeks. There was no history of diarrhea or dysentery. He served in the Southwest Pacific and the Philippine Islands from 1944 to 1945. His temperature on admission was 101.2 degrees F. Tenderness in right upper quadrant, and right pleural effusion were noted on February 14. Eight hundred cc. of lemon-colored fluid were aspirated from the right chest on February 26. The following day he experienced severe abdominal pain and generalized abdominal tenderness. Emetine hydrochloride therapy was started on February 28 and a laparotomy was performed. Generalized peritonitis, a subdiaphragmatic abscess and a liver abscess were found. The abscesses were drained. Postoperatively a

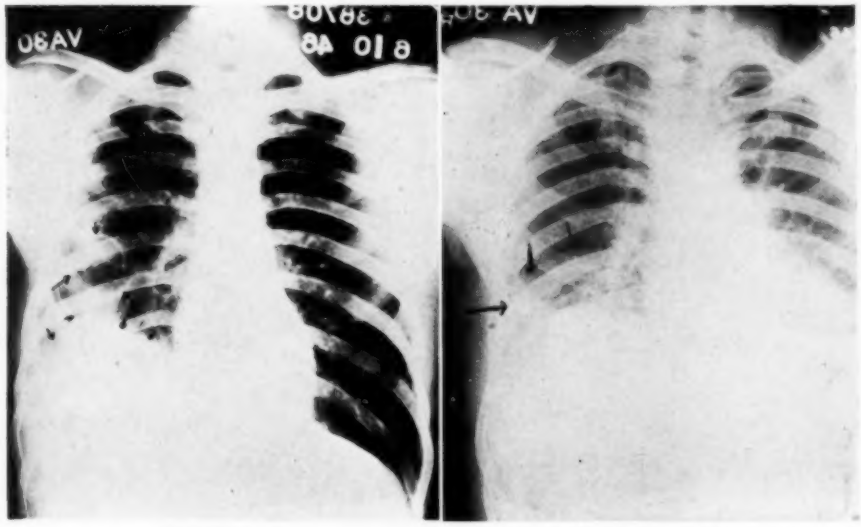


FIGURE 13 FIGURE 14

Fig. 13, Case 7: Elevation of right hemidiaphragm with contiguous pulmonary involvement.—*Fig. 14, Case 8:* Moderate elevation of right hemidiaphragm with contiguous pulmonary involvement.

course of emetine was completed and therapy continued with vioform, blood transfusions and daily irrigations of the operative wound. Following surgery, his temperature gradually fell to normal within two weeks. Intermittent fever recurred in May. It subsided after the administration of a second course of emetine and remained within normal limits the remainder of his stay. The anemia was improved by blood transfusions and iron therapy. Two additional chest taps for removal of fluid were necessary. Laboratory studies of the stools, and pus from the chest and abscess were all negative. The patient was discharged on June 18, 1946 as clinically well.

The most important extra-intestinal sites of amebiasis are the liver, lung and brain. The complications occur most frequently in the order listed.[2] Liver abscess is said to occur in about 20 per cent of the cases of amebic dysentery.[3] Approximately 35 per cent of the fatal cases have hepatic amebiasis.[2,4] Pleuro-pulmonary complications occur in about 15 per cent of patients having amebic hepatitis or abscess.[5]

The posterior-superior part of the right lobe of the liver is the favorite site for the amebic abscess in 70 per cent of the cases of hepatic amebiasis. It may rupture into the right pleural cavity, lung, or into the peritoneum. Another 15 per cent occur in the left lobe of the liver and may perforate into the left lung, pericardium, stomach or lesser sac of the peritoneum.[6] Pulmonary amebiasis may occur independently of hepatic abscess.[7] Whether primary or secondary, it closely simulates such pulmonary conditions as pleurisy with effusion, pneumonia, lung abscess, and tuberculosis. The rupture of a hepatic abscess into the lung may

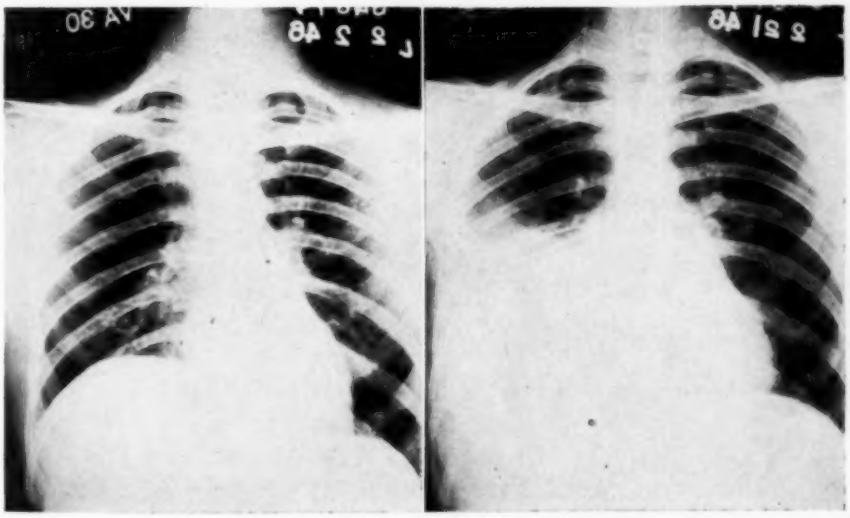


FIGURE 15 FIGURE 16

Fig. 15, Case 10: Elevated right hemidiaphragm without pleuro-pulmonary involvement.—*Fig. 16, Case 10:* Rupture of liver abscess into pleural space.

sometimes be the first evidence of its existence.[7] The mortality rate for the diagnosed abscess group ranges from 1 per cent[8] to 5 per cent.[9] Prognosis is poor and mortality rate is high when multiple liver abscesses are present.[4]

The diagnosis of thoraco-hepatic amebiasis usually rests on one or more of the following criteria: (1) suspicious symptoms, physical findings and suggestive roentgenograms or fluoroscopy showing a domed elevation and fixation of the right hemidiaphragm with or without continguous pleuro-pulmonary involvement, (2) typical proctoscopic findings, positive stools or positive sputum, and (3) therapeutic response to emetine.

The treatment of amebic abscess of the liver is both medical and surgical in most instances. Incomplete medical treatment alone results in too many relapses to be considered satisfactory. All unruptured amebic liver abscesses should be aspirated if possible after the institution of emetine therapy, preferably after the fourth or fifth day. This diminishes the possibility of seeding and removes the bulk of the involved material which presumably is one of the causes of relapses after medical therapy. Open drainage of amebic abscess of the liver is seldom indicated unless there is a complicating pyogenic infection.[4]

The treatment of complications of amebic abscess of the liver should be handled surgically with medical treatment maintained throughout the course of surgical management. The more common complications is rupture of the abscess into the abdominal cavity or rupture through the diaphragm into the thoracic cavity. Rupture into the abdominal cavity demands immediate surgical interference to provide drainage to the abscess bed.

Rupture through the diaphragm into the thoracic cavity may be of two types:

(a) Rupture into the free cavity which results in a very rapid total amebic empyema without appreciable involvement of the underlying lung. This requires a wide thoracotomy through the bed of the 7th or 8th rib so that all the debris may be cleaned out of the thoracic cavity. The hole through the diaphragm should be enlarged if necessary and abscess cavity wiped clean of debris. The diaphragm should then be repaired and drainage to the abscess cavity provided subdiaphragmatically. When the rupture has occurred more than four weeks prior to thoracotomy, decortication of the lung may be necessary. This will be determined by the degree of expansion of the affected lung under positive pressure by the anesthetist. Air tight intercostal underwater drainage or suction should be instituted postoperatively and continued as long as drainage occurs.

(b) When rupture occurs through diaphragm in the absence of a free pleural space, erosion is likely to continue into the lung parenchyma and bronchus with a resultant broncho-hepatic fistula. History of the coughing up of chocolate material is obtained and roentgenologic examination reveals parenchymal involvement of the right lower lung, contiguous to a domed diaphragm.

Wide thoracotomy is advisable, as in the previous type, except that in addition, the diseased lung must be treated by segmental resection of the involved portions of the lower or middle lobes. Whenever possible, this should be done by beginning with the bronchial division and carrying the dissection distally from this point rather than attempting resection by clamping off what appears to be the involved segments. It is usually impossible to judge the actual involved area, and by using clamps one tends to either leave diseased bronchi and lung tissue or to cut across normal bronchi. When the involved lung has been resected, the opening in the diaphragm should be enlarged if necessary to clean out the liver abscess and repair the diaphragm over subdiaphragmatic drainage. Since there is, as a rule, little appreciable pulmonary collapse from empyema in this type of rupture, decortication is rarely necessary.

SUMMARY

1) Ten cases of thoraco-hepatic amebiasis are presented. Five of these cases were proven by isolation of the causative organism and the remainder were diagnosed on presumptive clinical and operative findings. Adequate clinical response to therapeutic management was observed in eight patients. In one instance, thoraco-hepatic amebiasis was not diagnosed until necropsy. One patient left against medical advice and could not be completely studied.

2) The most common locale for the original infestation with E. Histolytica was the Pacific area, however, three patients who never left the continental limits of the United States, were found to have systemic amebiasis. It is pointed out that each imported case of parasitic infestation may be a source for endemic spread of the disease.

3) The frequent absence of intestinal symptomatology in the clinical history, and the preponderance of chest symptoms with right upper abdominal pain, as the presenting major complaints, was striking. The observation of changes in the chest teleoroentgenograms was occasionally diagnostic, and as a rule, appreciably helpful in arriving at the proper clinical evaluation.

4) The medical and surgical management of thoraco-hepatic amebiasis as a complication of systemic infestation, is discussed.

RESUMEN

1) Se presentan diez casos de amibiasis tóraco-hepática. Se comprobaron cinco de estos casos mediante el aislamiento del gérmen causante y los restantes fueron diagnosticados por los hallazgos clínicos y operatorios presuntivos. En ocho pacientes se observó una adecuada respuesta clínica al tratamiento. En un caso no se diagnosticó la amibiasis tóraco-hepática sino en la autopsia. Un paciente se salió sin permiso médico y no se le pudo estudiar completamente.

2) El lugar más común donde se originó la infestación con E. histolitica fue la zona del Pacífico. Empero, se descubrió amibiasis orgánica en tres pacientes que nunca habían salido de los límites continentales de los Estados Unidos. Se indica que cada caso de infestación parásita importada puede conducir a la extensión endémica de la enfermedad.

3) Fue sorprendente la frecuente ausencia de sintomatología intestinal en la historia clínica y la preponderancia de síntomas torácicos, y de dolor en la parte superior del abdomen, entre las principales quejas iniciales. Ocasionalmente la observación de alteraciones en los teleroentgenogramas torácicos estableció el diagnóstico y, por lo general, estas películas ayudaron a arribar al avalúo clínico apropiado.

4) Se discute el tratamiento médico y quirúrgico de la amibiasis tóraco-hepática como complicación de la infestación general.

REFERENCES

1 "Report of Epidemiology Unit No. 11," Bureau of Medicine and Surgery, Navy Department, September 1945 (unpublished).
2 Craig, C. F.: "The Etiology, Diagnosis and Treatment of Amebiasis," *Williams and Wilkins Co.*, Baltimore, 1944.
3 Strong, R. P.: "Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases," *The Blakeston Co.*, Philadelphia, 1944.
4 Ochsner, A. and De Bakey, M.: "Amebic Hepatitis and Hepatic Abscess; Analysis of 181 Cases with Review of Literature," *Surgery*, 13:460, March; 612, April 1943.
5 Ochsner, A., De Bakey, M., Kleinhasser, L. R. J. and De Bakey, E.: "Amebic Hepatitis," *Rev. Gastroenterol.*, 9:438, 1942.
6 Bingham, D. L. C.: "The Treatment of Some Surgical Complications of Amebiasis," *Canadian M. A. J.*, 55:341, 1946.
7 Manson-Bahr, P.: "Pulmonary Amebiasis," *Lancet*, 2:599, 1923.
8 Cort, E. C.: "Amebiasis of the Liver," *J.A.M.A.*, 90:2005, 1928.
9 Sodeman, W. A. and Lewis, B. O.: "Amebic Hepatitis, Report of 33 Cases," *J.A.M.A.*, 129:99, 1945.

Benign Pleural Effusion and Ascites Associated with Adenocarcinoma of the Body of the Pancreas*

EMIL ROTHSTEIN, M.D., F.C.C.P.
Wood, Wisconsin

In 1937, Dr. Joseph V. Meigs[1] of Massachusetts General Hospital brought to the attention of the medical profession the not infrequent occurrence of pleural effusion and ascites associated with benign ovarian tumors. Cases thought to be hopeless because of alleged pleural metastasis (postulated upon the finding of unilateral or bilateral pleural effusions) were cured by oophorectomy; after this surgical procedure the effusions were spontaneously and permanently absorbed. Meigs' syndrome has been reported in association with various sorts of ovarian tumors, including fibromata (the subject of Meigs' original report), cystadenoma, thecoma, granulosa cell tumor and Brenner tumor, as well as with uterine fibromata. About fifty cases of this syndrome have been reported to date. Two recent articles, containing reviews of the literature and bibliography, are those of Calmenon, Dockerty and Bianco[2] and Nora and Davison.[3]

I have been unable to find any reports of a similar syndrome in association with any tumors other than those of the female genitalia. The case which gave rise to the present report presents a similar syndrome in a male patient with a carcinoma of the body of the pancreas. This offers a challenge to the internist and the surgeon, since, just as in the case of Meigs' syndrome, the presence of recurring pleural effusions with ascites was considered evidence of hopeless metastasis.

Case Report: The patient was a 58 year old man who entered Wood Veterans Hospital April 3, 1947. In the summer of July 1946 he had coronary thrombosis, necessitating two months of hospitalization. At this time mild diabetes mellitus was discovered, which was controlled by diet alone. The complaints upon his last admission were referred chiefly to the chest and consisted of dyspnea, chest pain, cough and expectoration. All had been present for ten weeks. Upon examination he appeared

*From the Medical Service, Veterans Administration Hospital, Wood, Wisconsin, Mark Garry, M.D., Chief of Service, with whose permission and cooperation this case is reported.
Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

chronically ill and presented the findings of a bilateral pleural effusion. In addition, a rounded mass was discovered in the left upper quadrant of the abdomen. This was about 8 cm. in diameter, firm and not tender, and moved slightly with respiration. Moderate hypertension was present. Laboratory tests revealed the following pertinent findings: Diabetic type of glucose tolerance curve; slight anemia; sedimentation rate of 11 mm.; total plasma protein 6.6 gm. per cent; plasma albumin 5.1 gm. per cent; and an ECG showing myocardial damage on the basis of T-wave changes. There was x-ray evidence of a bilateral pleural effusion (Fig. 1). In addition x-ray findings were indicative of an extrinsic mass 8 cm. in diameter displacing the stomach anteriorly and to the left. These findings were considered to indicate a carcinoma of the body of the pancreas with extensive pleural and peritoneal metastases. The clinical course was steadily downhill. The pleural effusions were aspirated repeatedly but recurred. The fluid was cloudy and amber. No tumor cells, tubercle bacilli, or other bacteria were found. About three weeks after admission, leg edema and marked ascites developed. A second total protein was 4.5 gm. per cent with albumin of 2.7 gm. per cent. After one of the numerous thoracenteses a traumatic left pneumothorax developed and despite repeated decompressions the patient presented progressive dyspnea and shock and expired on July 23, 1947.

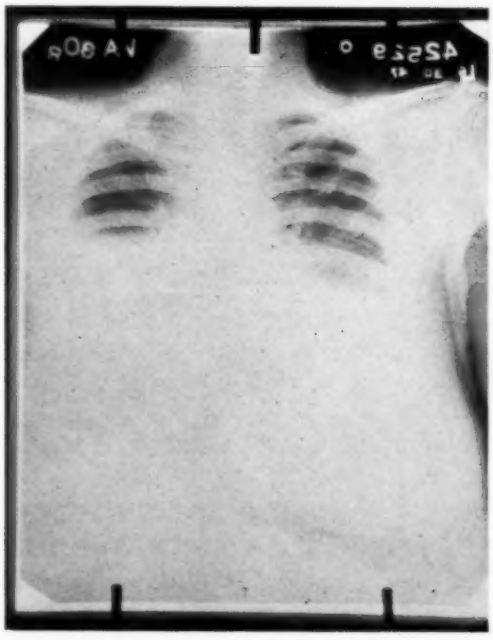


FIGURE 1

Autopsy (Dr. A. Swingle): The pertinent findings were as follows: The tumor was a cystic adenocarcinoma of the body of the pancreas. The only metastases were two minute nodules in the liver, measuring 1 and 4 cm. respectively. Microscopically these were identical with the main tumor mass. The peritoneum was grossly normal and free of any metastatic deposits. Two thousand cc. of reddish yellow fluid were present. The omental veins were markedly distended and tortuous as were the inferior mesenteric veins and other branches of the portal system. Both pleurae

were entirely free, grossly and microscopically, of any tumor tissue. Bilateral pleural effusion was found and in addition there was a tear in the collapsed left lung. The heart presented an old healed infarction in the lower portion of the left ventricle and the apex.

Discussion

This patient had a large well encapsulated carcinoma of the body of the pancreas. Two small metastatic nodules were present in the liver. While the age of these nodules cannot be determined one may assume from their small size that they may have been of recent origin. It is not unreasonable to suppose that a tumor of this sort could have been extirpated in toto before metastases occurred. This is dependent upon ruling out distant metastases preoperatively. In the past, pleural effusion, in the presence of an abdominal tumor has been considered evidence of hopeless metastasis. May it not be that this situation will change in a manner similar to that now current in the field of gynecological surgery? Until Meigs clarified the benign nature of pleural effusion in the course of pelvic tumors a number of otherwise operable cases were denied surgery because of the presumably fatal significance of this finding. Perhaps the same benign evaluation may, at least occasionally, be given to the presence of pleural effusion accompanying other abdominal tumors.

The mechanism of the ascites in this case can probably be explained by the large tumor mass in the pancreas causing obstruction to the return venous circulation of the portal system. After the ascites developed, the low blood protein was a factor in the development of generalized edema. The extensive hydrothorax, recurring as it did, in the absence of any evidence of obstruction to the azygos vein or to the superior vena cava presented a much more difficult problem. In the numerous articles on Meigs' syndrome (for I assume the mechanism is probably similar in this case) several explanations are given. None of these explanations fits all of the facts nor satisfies the authors who propose them and I am unable to clarify that question here. Several cases have had the serum proteins studied, but as in this case, (upon the first examination) they were essentially normal. Air introduced into the pleural space or into the peritoneal cavity was not found to go through the diaphragm into the neighboring cavity.[2,3] India ink particles introduced into the abdomen have been found in the pleural fluid 48 hours later.[2,3] In several cases reported in the literature, examination of the two fluids has shown that they are apparently identical as to protein content and other chemical constituents. These last two observations seem to indicate that the two fluids are derived from a single source and it is believed that the ascitic fluid may reach the pleura

via diaphragmatic lymphatics. The direct relation between the effusions and the pelvic tumors has been established by the fact that the fluid recurs after repeated aspirations but upon removal of the tumor the fluid is absorbed rapidly and permanently. Perhaps some pathogenetic significance may lie in the fact that of the pleural effusions in Meigs' syndrome about 80 per cent are right-sided, about 10 per cent left sided, and the remainder bilateral.

SUMMARY

A case has been presented which was characterized by the presence of bilateral pleural effusion and ascites in the presence of an abdominal tumor. At autopsy the tumor was found to be a pancreatic carcinoma with two small and probably recent metastases in the liver. The effusions were found to be due to causes obscure in nature but not carcinomatous in origin. It is suggested that this case may be analogous to cases of Meigs' syndrome, associated with a pancreatic tumor. Every procedure should be exhausted to demonstrate the benign or malignant nature of the effusions in this type of syndrome. If pleural metastases cannot be demonstrated and the abdominal tumor is amenable to surgery such surgery would then seem to be indicated.

RESUMEN

Se ha presentado un caso caracterizado por la presencia de derrame pleural bilateral, ascitis y tumor abdominal. Durante la autopsia se descubrió que el tumor fue un carcinoma pancreático con dos pequeñas metástasis en el hígado, probablemente de origen reciente. Se descubrió que los derrames se debieron a causas obscuras, pero no de origen carcinomatoso. Se sugiere que este caso puede ser análogo a casos del síndrome de Meig asociados con un tumor pancreático. Deben agotarse todos los procedimientos a fin de demostrar la naturaleza benigna o maligna de derrames en este tipo de síndrome. Si no se pueden demostrar metástasis pleurales y el tumor abdominal es tratable por medios quirúrgicos, parecería que está indicada la operación.

REFERENCES

1 Meigs, J. V. and Cass, J. W.: "Fibroma of the Ovary with Ascites and Hydrothorax with Report of Seven Cases," *Am. J. Obs. and Gyn.*, 33: 249, 1937.
2 Calmenson, M., Dockerty, M. B. and Bianco, J. J.: "Certain Pelvic Tumors Associated with Ascites and Hydrothorax," *Surg., Gyn. and Obs.*, 84:181, 1947.
3 Nora, F. D. and Davison, R. M.: "Pleurisy with Effusion Associated with Pseudomucinous Cystadenoma (Meig's Syndrome)," *Dis. of Chest*, 13: 423, 1947.

Tuberculosis and Carcinoma of the Lung

ARCHIBALD C. COHEN, M.D., F.C.C.P.*
Butler, Pennsylvania

The co-existence of pulmonary tuberculosis and bronchiogenic carcinoma was first reported by Bayle in 1810,[1] and by 1940 a total of only about sixty cases had been reported.[2] Reports have been more frequent in the past few years,[3-5] indicating either an actual increase in the co-existence of these two diseases or an increasing awareness of the existence of one disease in the presence of the other. However the diagnosis in most cases is still made at necropsy. It is the object of this paper to describe three more cases seen recently, principally to stimulate physicians to be alert to the possibility of the existence of carcinoma in cases of pulmonary tuberculosis which are behaving atypically.

Case 1: The patient, a 52 year old white man, was admitted on June 16, 1942. His paternal grandfather died of carcinoma; four close relatives (two maternal uncles and two maternal aunts) died of pulmonary tuberculosis. He felt well until about two weeks before admission, when he suddenly developed cough, fever, chills, and pain in the right lower chest. From then on, he lost weight and became weak. Physical examination showed poor nourishment (height 70 inches, weight 120 lbs.). Chest was symmetrical and expansion equal on both sides. Fremitus, resonance, breath sounds, spoken and whispered voice were normal; there were no rales, rhonchi, or friction rubs. X-ray film of the chest showed soft shadows in the right lung, from the first to the fourth interspaces anteriorly. Temperature was slightly elevated, never above 100 degrees F. Sputum was scanty, and repeated concentration failed to reveal tubercle bacilli. Gastric lavage was performed on July 2, 1942; smear of gastric contents was negative, but on culture there was growth of typical colonies, and smear from the culture on July 31, 1942 revealed tubercle bacilli. Patient left the hospital against medical advice at this time. In August he noticed swelling of the neck, dyspnoea on slight exertion, and discoloration of the skin over the chest. Early in October he returned to the hospital. He was bronchoscoped and a biopsy specimen was taken; the laboratory report on tissue removed from the right main bronchus was "bronchiogenic carcinoma, squamous-cell type." In October, both arms began to swell and in November, both ankles began to swell. Examination by the thoracic surgeon at that time showed that the case was inoperable; patient was dyspnoeic and cyanotic at rest; veins of thorax, abdomen, and both arms were engorged; there was diffuse swelling of the tissues of the lower neck; there was considerable edema of the arms

*From the Veterans' Administration Hospital, Butler, Pennsylvania. Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans' Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

(more on the right), and slight edema of the ankles; the pulse in the right arm was weaker than in the left; the axillary nodes were bilaterally enlarged, firm, and fixed, and the trachea was deviated to the left. Examination of the lungs revealed flatness, absent fremitus, and absent breath sounds on the right, and hyperresonance on the left. The abdomen was soft. The liver was palpable 3 cm. below the right costal margin, and was nodular. Rectal examination was negative. Laboratory data: Stool examination was positive for occult blood; gastric contents showed no free hydrochloric acid, but did contain occult blood; gastrointestinal series showed deformity of the duodenal bulb; radiograph of the chest revealed the heart and mediastinal contents slightly displaced to the left, with a massive effusion on the right. Thoracocentesis was performed on November 18 and 2,000 cc. of fluid were aspirated from the right chest. Three deep x-ray treatments were given, but dyspnoea and cyanosis became progressively worse and the patient died on November 20, 1942. Necropsy was not performed. Clinical diagnoses:

1) Bronchiogenic carcinoma with extensive metastases to the mediastinum, liver, and axillary lymph nodes.
2) Pulmonary tuberculosis.

Case 2: A 53 year old negro laborer was admitted on April 24, 1943, complaining of inspiratory pain in the right hemithorax, cough, expectoration, hemoptysis, and loss of weight and strength. Past and family history were negative. Examination showed an emaciated negro male lying quietly in bed, dyspnoeic and in pain. There was dullness to percussion, diminished but bronchial breath sounds and whispered pectoriloquy from the apex down to the third dorsal vertebra posteriorly and the fifth rib anteriorly; no rales, rhonchi, or friction rub. The heart was normal and in normal position; blood pressure was 112/72. The temperature was irregular, but rose as high as 102.6 degrees F. X-ray film showed homogeneous density filling nearly the entire right pleural space with the exception of small areas of aeration at apex and base. The urine was normal; blood count was normal; blood Wassermann was negative; and sputum concentrates were repeatedly negative for tubercle bacilli. On April 28, 1943 a needle was inserted into the right pleural space in the ninth interspace posteriorly, and 400 cc. of thin but turbid yellow fluid aspirated. The fluid was negative on smear, but guinea pig inoculation revealed tubercle bacilli; as a result the diagnosis of pleurisy, serous, right, tuberculous, was made. Pain was constant and became increasingly severe. Dyspnoea became a prominent symptom. The patient assumed a peculiar posture, lying flat in bed, motionless, face downward, with rapid and shallow respiration. The right hemithorax became definitely larger than the left, but moved very little on respiration. Repeated attempts to aspirate fluid from the right hemithorax failed. X-ray film of the chest taken May 25, 1943 showed the entire mediastinal contents displaced to the left, the interspaces widened on the right, and an extensive area of homogeneous density almost filling the right hemithorax. On May 26, 1943 a large gauge aspirating needle was inserted into the right lung high in the posterior axillary line and 4 cc. of soft granular tissue was aspirated. Microscopic examination revealed bronchiogenic carcinoma. Patient refused further treatment and left the hospital on June 3, 1943; on July 1, 1943 he died at home. Diagnoses:

1) Carcinoma, bronchiogenic, right lung.
2) Pleurisy, serous, tuberculous, right.

Case 3: Patient, a 59 year old white man, was admitted on March 4, 1947. Family and past history was irrelevant. In the year prior to admission he had become weak and had lost thirty pounds weight. In the three months prior to admission he had noticed vague soreness in the right chest, slight dyspnoea, and cough; the cough was at first non-productive, then productive of a small amount of serous sputum, and finally productive of about an ounce daily of mucopurulent sputum. Three days before admission he became hoarse. Physical examination showed a markedly emaciated white man (height 5 feet 11¾ inches, weight 130 lbs.). Temperature was 101.4 degrees F., pulse 100, respirations 22. Blood pressure was 90/70. Resonance was impaired and fremitus decreased over the upper third of the left lung. On admission, x-ray film revealed atelectasis of the left upper lobe; the left diaphragm was elevated but moved on respiration; there was a mass 4cm. in diameter in the left hilum. The left vocal cord was found to be paralyzed on mirror examination and this finding was confirmed by laryngoscopy. A provisional diagnosis of inoperable bronchiogenic carcinoma, with involvement of the left recurrent laryngeal nerve, was made on admission. Sputum was repeatedly positive for tubercle bacilli on direct smear. Bronchoscopy was attempted three times, but was unsuccessful each time; the patient was apprehensive and poorly relaxed, so that visualization of the bronchial tree was not possible. Serial x-ray films showed extension of the atelectasis and of the hilar mass. On April 30, 1947, the whole left lung was found to be obscured, with retraction of the heart and mediastinal contents to the left. Thoracocentesis showed hemorrhagic fluid. He became steadily more dyspnoeic in spite of repeated thoracocenteses; he became cyanotic and pain became severe, so that he required oxygen and morphine. He died on May 28, 1947. Necropsy was refused. Diagnoses:

1) Carcinoma, bronchiogenic, left lung (tentative).
2) Tuberculosis, pulmonary, chronic, active.

Discussion

Pulmonary tuberculosis is still a common disease, in spite of the progress which has been made toward its control in recent years, and is being recognized fairly frequently in people past middle age. Carcinoma of the lung has been diagnosed with increasing frequency in the past decade, both clinically and at post-mortem examination. It is therefore to be expected that the incidence of the combined diseases, tuberculosis and carcinoma of the lung, should be reported more and more often, and this has been the fact in the past few years. There is a possibility that advancing carcinoma may invade healed foci of tuberculosis in which virulent tubercle bacilli survive; in such cases the freed tubercle bacilli would be responsible for a positive sputum and might cause tuberculous disease of the lung. It is believed that this was the sequence of events in Case 3 in which both clinically and roentgenologically all the evidence pointed to bronchiogenic carcinoma from the beginning and the diagnosis of tuberculosis was entertained only after the discovery of tubercle bacilli in the

sputum. Rousseau and Coté[6] believe that carcinoma may produce anergy to tuberculin, thus favoring exacerbation of an arrested tuberculosis. Theoretically there is another way in which carcinoma may favor the development of active tuberculosis; that is, by producing general debility. Matz[7] believes that pulmonary tuberculosis or any other chronic disease of the respiratory tract, causes irritation of the respiratory tract which in some cases results in proliferation of the bronchial mucosal cells and metaplasia. In most cases the coexistence of these two diseases is probably mere chance.

When carcinoma is present in a tuberculous patient, it is important to make the diagnosis early so that pneumonectomy can be done with some prospect of success. The diagnosis is more difficult than in a nontuberculous patient, because the symptoms produced by the carcinoma are explained in the mind of the physician as being due to tuberculosis. If the physician will bear in mind the possibility of carcinoma in such cases, the correct diagnosis will be made much more often. In spite of a proven diagnosis of tuberculosis, if the symptoms are out of proportion to the size of the lesion, if there is unexplained dyspnoea or pain, if there is a change in the character of the cough and expectoration, and above all if x-ray shows an area of atelectasis, cancer should be suspected. The suspicion of cancer should cause the physician to secure at once: bronchoscopy, cell block of sputum and pleural fluid, and biopsy of possible metastatic nodes. In Case 1 carcinoma should have been suspected in August instead of October; energetic institution of diagnostic procedures at that time might have brought the patient to the surgeon while pneumonectomy was feasible, whereas three months later he was inoperable.

SUMMARY

1) Three cases are reported of co-existing tuberculosis and carcinoma of the lung. All cases were diagnosed during life; all cases were diagnosed too late for surgery.

2) The diagnosis of carcinoma in the presence of pulmonary tuberculosis depends on the same studies as in the absence of tuberculosis—x-ray, bronchoscopy, cell-block of sputum and pleural fluid, biopsy of suspected metastatic nodes, and exploratory thoractomy. The history is of diminished value, because the symptoms may be caused by tuberculosis as well as by carcinoma.

3) Carcinoma should be suspected when symptoms are out of proportion to the size of the tuberculous lesion, when there is unexplained dyspnoea or pain, or when x-ray shows an area of atelectasis. The diagnosis of carcinoma in the presence of pul-

monary tuberculosis is usually made too late because it is not suspected.

RESUMEN

1) Se informa sobre tres casos de tuberculosis y carcinoma del pulmón coexistentes. Se diagnosticó a todos los casos durante la vida, pero demasiado tarde para la intervención quirúrgica.

2) El diagnóstico de carcinoma en la presencia de tuberculosis pulmonar depende de los mismos estudios que en la ausencia de tuberculosis, a saber, radiografía, broncoscopia, exámenes de células en el esputo y el derrame pleural, biopsia de ganglios metastásticos sospechados y toracotomía exploratoria. La historia tiene menos valor, porque los síntomas pueden ser causados por tuberculosis lo mismo que por carcinoma.

3) Se debe sospechar carcinoma cuando los síntomas están fuera de proporción al tamaño de la lesión tuberculosa, cuando existen disnea o dolor inexplicables o cuando la radiografía revela una zona de atelectasia. Generalmente se hace demasiado tarde el diagnóstico de carcinoma en la presencia de tuberculosis pulmonar porque no se le sospecha.

REFERENCES

1 Bayle, G. L.: "Recherches sur la phthisie pulmonaire," Paris, *Gabon,* 1810, page 315.

2 Hamilton, C. E. and Wexler, N. H.: "Carcinoma and Tuberculosis of the Lung," *Am. Rev. Tuberc.*, 42:334, 1940.

3 De la Fuente, M. A. and Palacious, H. R.: "Undifferentiated Cell Carcinoma of Lung and Chronic Pulmonary Tuberculosis," *Quart. Bull. Sea View Hosp.*, 7:314, 1942.

4 McCorkle, R. G., Koerth, C. J. and Donaldson, J. M. Jr.: "Carcinoma and Tuberculosis of Lung," *Med. Rec.*, 155:213, 1942.

5 Gerstl, B., Warring, F. C. Jr. and Howlett, K. S. Jr.: "Cancer and Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 54:470, 1946.

6 Rousseau, L. and Coté, G. L.: "Cancer bronchique et tuberculose pulmonaire associés," *Laval Med.*, 7:445, 1942.

7 Matz, Philip B.: "Incidence of Primary Bronchiogenic Carcinoma," *J.A.M.A.*, 111:2086, 1938.

Idiopathic Spontaneous Hemopneumothorax*

An Evaluation of Its Treatment and Report of Three Cases

WALTER L. NALLS, M.D., F.A.C.P., F.C.C.P.
Oteen, North Carolina

JAMES H. MATTHEWS, M.D.
Asheville, North Carolina

Idiopathic spontaneous hemopneumothorax is recognized clinically when intrapleural hemorrhage occurs in association with a spontaneous pneumothorax in otherwise apparently healthy individuals and is unrelated to trauma, malignancy, therapeutic pneumothorax, tuberculosis or other demonstrable disease of the lungs. Its close relationship with spontaneous pneumothorax is emphasized by its occurrence in individuals who have previously sustained an idiopathic spontaneous pneumothorax.[1] More significantly than in simple spontaneous pneumothorax, however, spontaneous hemopneumothorax is a grave emergency which requires prompt treatment because of the added threat of exsanguination superimposed on the cardiorespiratory disturbance resulting from collapse of a lung. A case fatality rate of about 30 per cent, death usually occurring within the first 24 hours, as reported by Hartzell[1] in 1942, should be subject to reduction in the light of current concepts of treatment if courageously applied.

The incidence of this condition is considered rare. Hartzell[1] in 1942 was able to find only 44 cases recorded, including those reported in his paper. Subsequently reports of 11 cases have appeared.[2-11] This probably does not represent the true incidence. Hartzell[1] reported four cases, Waring[9] had seen two and Hopkins[12] treated three. Three cases are reported here, all of which were observed within less than six months. One of us has seen an additional case not included in this report and we have knowledge of at least five other unreported cases.[13,14] It seems not unlikely that any physician may be called upon to recognize and treat this interesting condition. That life may depend on the physician's success is well shown by the case reported by Helwig and Schmidt[2] and by the first case reported here.

---

*From the Department of Medicine and Surgery, Veterans Administration, Oteen, North Carolina; published with permission of the Chief Medical Officer, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

The pathogenesis, pathology and a detailed description of the clinical characteristics of spontaneous hemopneumothorax will not be discussed here as they have been adequately presented previously[1] and are now less controversial than the treatment. For this report, it is accepted that the bleeding results from vascular damage, whether at the time of onset of a spontaneous pneumothorax or subsequently as collapse increases and adhesions are torn. It is of some significance to realize that the bleeding vessel may be in the parietal pleura where it is not subject to control as collapse of the lung increases. It is also accepted that the persistent fluid state of the blood has been demonstrated to result not from a theoretical anticoagulant effect of the pleura but rather from rapid defibrination by cardiorespiratory action, resulting in a deposition of fibrin on the pleural surfaces. This is to be reckoned with in treatment if bleeding has been extensive. Determination of clotting properties of the aspirated blood may be used to decide whether bleeding has stopped. If there is still active bleeding, it is likely that the blood will clot on removal, whereas if bleeding has ceased and all the blood has been defibrinated, no clot will form.

Principles of treatment may be established for hemopneumothorax but the treatment of individual cases will of necessity depend on the nature and severity of the clinical manifestations. Several interrelated conditions exist. Sudden collapse of a lung disturbs the pulmonary circulation and reduces the oxygen saturation of the blood. Elevated intrathoracic pressure interferes with venous blood flow to the heart resulting in reduced cardiac output. Hemorrhage into the pleural cavity increases the degree of collapse of the lung and at the same time reduces the blood volume and the oxygen-carrying capacity of the blood. This also contributes to loss of cardiac output and produces hypotension. The ill effects from hemorrhage and from tension pneumothorax augment each other so that compensatory mechanisms are impaired. If bleeding is severe, profound and irreversible shock may develop rapidly unless active treatment is instituted. Reliance on a high intrathoracic pressure and low systemic blood pressure to stop the bleeding as suggested by numerous writers[1,4,6] may result in further unjustified mortality.

Treatment as outlined by Waring[9] in 1945 is more rational than that recommended by earlier authors. Aspirations of air and blood should be performed early and often enough to avoid high intrapleural pressure with resultant circulatory and respiratory embarrassment and mediastinal displacement. Replacement of air for blood aspirated, at this stage at least, is irrational. Transfusions should be given to maintain adequate blood pressure and

hemoglobin levels. The use of blood aspirated from the chest for transfusion has not been advised. Waring[9] has argued against it, stating that hemolysis and possible infection of the blood present a danger. However, if use of this blood may be lifesaving while donors are being obtained, as in the first case reported below, it is amply justified. Oxygen may be given as necessary in the acute period and rest and sedation should be maintained. When uncontrolled hemorrhage persists, thoracotomy has been suggested,[9] although we find no case recorded in which this procedure has been necessary. During the early period after the onset of a hemopneumothorax, the greatest danger of such a program of active treatment is the risk of infection from multiple aspirations. This can be reduced by the use of antibiotic drugs and should not constitute a handicap if such treatment can significantly reduce the mortality.

Once the acute phase is over and bleeding has stopped, different considerations govern the therapy. Shock and sudden death are not a problem but the speed and extent of recovery are related to the therapeutic management. Anemia is still to be combatted especially if any operative procedure is required. Infection of the pleural space must be avoided, or treated if present. Early and complete reexpansion of the lung is the aim of treatment in this period. The success with which expansion is achieved depends first on the presence of infection and second on the extent of fibrin deposits on the pleura. It is well known that small sterile hemorrhages will absorb without any demonstrable residual pleuritis. Jennings[3] noted that this is less readily accomplished by an encapsulated interlobar collection of blood than by blood free in the pleural space. Early aspiration is probably more significant in obtaining reexpansion than is late removal of defibrinated blood. Replacement of air when blood is aspirated would be considered only if a high negative intrathoracic pressure resulted. Decortication of the lung may be required where earlier treatment has been inadequate as in the second case reported here. Finally, for the patient who has a dry residual pneumothorax with a lung that is expanding poorly, instruction by a skilled physiotherapist in unilateral breathing may be of value. Once reexpansion is complete, pleural symphysis is apparently obtained. At least there is no record of a recurrence of hemopneumothorax.

Many of the treatment principles presented as related to idiopathic spontaneous hemopneumothorax would apply similarly to other types of hemothorax and hemopneumothorax. The incidence of infection in traumatic hemothorax is greater and decortication is much more likely to be required. Spontaneous hemopneumothorax developing during the course of pneumothorax treatment

for tuberculosis raises problems in the maintenance of the collapse therapy which are not germane to this discussion.

CASE HISTORIES

Case 1: A 41-year-old white male was admitted to the hospital on the evening of November 6, 1946, complaining of pain in the left chest and shortness of breath. On the previous evening while driving a bus, he experienced a sudden pain in the left chest which radiated to the left shoulder and was accompanied by some shortness of breath. This was not preceded or accompanied by sneezing, coughing or other unusual exertion. Later in the evening the pain became more severe and he was treated symptomatically at his home. The following day he was worse and entered the hospital about 3:00 p. m., some 24 hours after onset of symptoms.

There was no history of tuberculosis or other pulmonary diseases in the family, nor were there any known contacts with tuberculosis. There was nothing of significance in the past medical history. A wife and one child were living and well. Some slight cough had been present for years, which he attributed to smoking.

Upon admission to the hospital he was obviously dyspneic, pale and in pain. He had had little or no rest since the onset of symptoms. The pain involved all of the left side of the chest, left shoulder and left side of the neck. There was some evidence of cyanosis. The mucosae were pale. There was fullness of the left hemithorax with widening of the interspaces and diminished expansion on this side. No cardiac pulsations were seen. The percussion note was hyperresonant over the left, except at the left base posteriorly, where resonance was impaired. Breath sounds were absent on the left and were exaggerated on the right side. No heart sounds were heard over the left. On percussion, cardiac dullness was found to be to the right of the sternum. Heart sounds, likewise, were found to the right of the sternum. The rhythm was regular. Rate was 128 per minute and sounds were of fair intensity. No murmurs were heard. The pulse was thready in character. Blood pressure: 90/75. The abdomen was flat, tympanitic and no tenderness or masses were noted.

Urinalysis revealed no abnormalities. Examination of the blood gave the following result: hemoglobin, 70 per cent; red blood cells, 3,600,000; white blood cells, 26,100. Polymorphonuclears, 88 per cent; lymphocytes, 10 per cent and monocytes, 2 per cent. An x-ray film of the chest (Fig. 1) showed complete collapse of the left lung with some herniation to the right side, and with marked shifting of the heart, trachea and mediastinum to the right. The film was made with the patient in bed in a semi-recumbent position, and the haziness over the left base was thought to be fluid. An electrocardiogram showed only a sinus tachycardia and some diminution of the amplitude of T-Waves in Lead 1.

The patient was given meperidine (demerol, Winthrop) 50 milligrams, for pain, with but little relief. His condition became rapidly worse and evidence of shock increased. The pain began to spread downward over the abdomen, and increased resistance was noted over the upper abdomen. About 7:00 p. m., a left thoracentesis was done. After removal of approximately 350 cc. of air, under increased pressure, blood appeared in the syringe. This confirmed the impression of hemopneumothorax. Aspiration was discontinued after the removal of approximately 20 cc. of blood. This did not clot. For a short time following this the patient

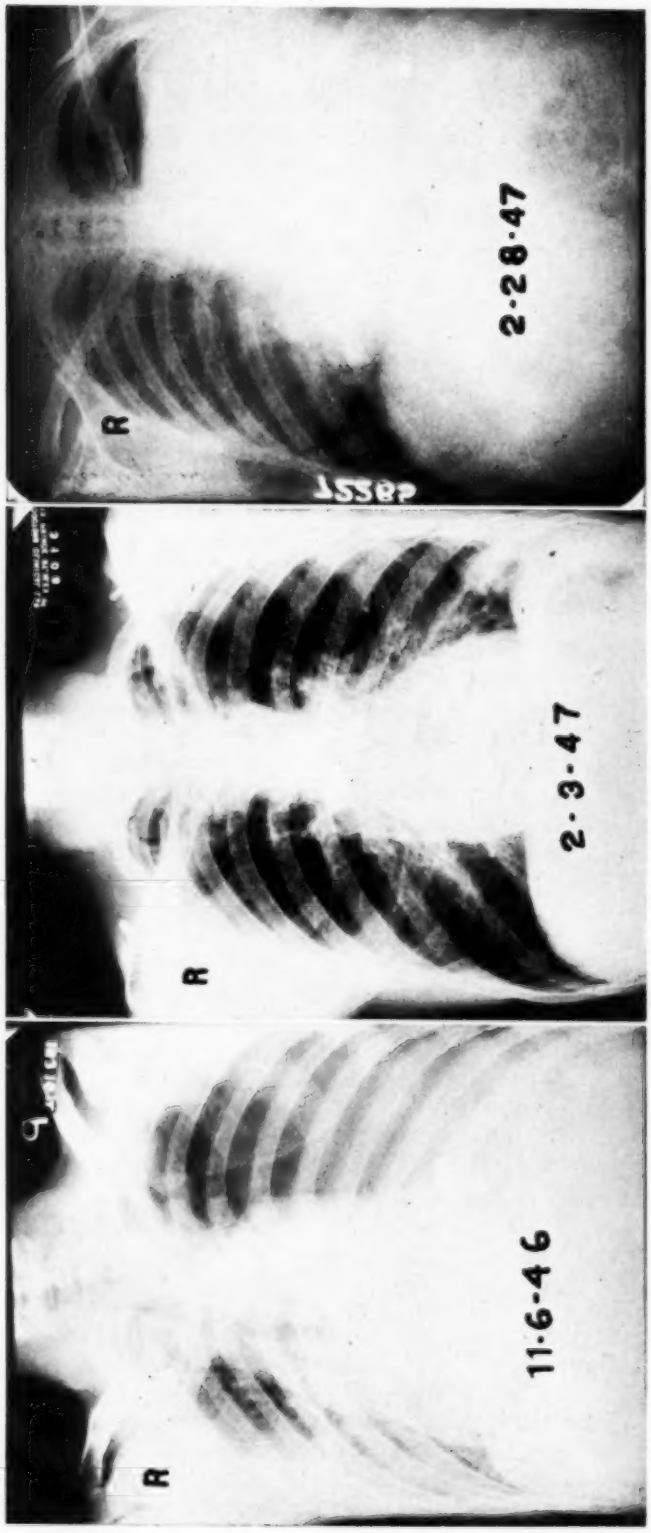


FIGURE 1

FIGURE 2

FIGURE 3

felt somewhat more comfortable, but by 9:00 p. m. he was again much worse and rapidly developed signs of collapse. He was seen by one of us about 10:00 p. m. At this point he was in extremis and there was every indication that he would expire before anything could be accomplished. A needle was inserted into the left pleural cavity and an unmeasured quantity of air was removed, after which he promptly regained consciousness. Oxygen therapy was begun by nasal catheter and blood obtained for typing. It was apparent that he had lost a large portion of his circulating blood into the left pleural cavity. Since the need for transfusion of whole blood was emergent, and since some delay was inevitable in obtaining compatible whole blood, it was decided to transfuse him with his own blood removed from the pleural cavity. Accordingly, blood was withdrawn from the left pleural cavity into transfusion flasks and given intravenously.

During the night the left pleural cavity was aspirated many times; sometimes air was removed, sometimes blood. The removal of air was determined by the patient's symptoms. On two or three occasions he lost consciousness, only to regain consciousness after removal of air. Frequent manometric readings were taken in order to keep the intrapleural pressure slightly positive. Altogether, approximately 1,800 cc. of blood was removed from the pleural cavity and given intravenously. The amount of air removed was not measured. In the meantime donor blood was obtained and given.

By morning the patient's condition was still critical, though we felt that bleeding had decreased. Hemoglobin estimation at this time was 58 per cent and the red blood count was 2,800,000, in spite of almost continuous transfusion. Because of the possibility of contaminating the pleura by frequent taps, administration of penicillin was begun, 30,000 units intramuscularly, and was also introduced into the pleural cavity after aspiration. The patient improved during the day and by evening was definitely better. Aspirations of blood and of air were continued as indicated. The second morning bleeding apparently had stopped. Aspiration on two occasions yielded only 75 and 125 cc. of blood. Pressure relations in the chest had become stabilized. The lung had begun to expand and the mediastinum and heart had begun to return to a normal position. The patient was much improved. Hemoglobin estimation at this time was 72 per cent; the red blood count was 3,400,000. Repeated sputum studies for acid-fast bacillus were negative.

From this point on, his course was that of gradual improvement. During the first few days his temperature varied irregularly between 99 and 102 degrees Fahrenheit. This returned to normal on the sixth hospital day and remained so except for occasional slight elevation. Penicillin intramuscularly was continued for several days after the temperature had returned to normal. He was then able to take a regular diet and his blood picture gradually returned to normal. Serial x-ray examinations of the chest showed gradual absorption of air and blood from the pleural cavity with return of the heart and mediastinum to normal position. He was discharged from the hospital three weeks after admission. At this time the lung had completely expanded. After a period of convalescence with slow return to activities, he was permitted to resume work three months after leaving the hospital, at which time there remained only some pleural shadows at the left base on chest films (Fig. 2). He had gained weight and felt quite well.

Comment: This case illustrates certain features which have been men-

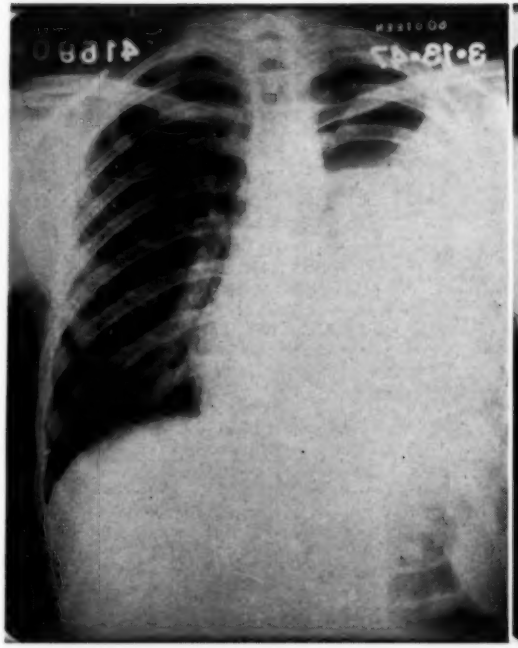


FIGURE 4

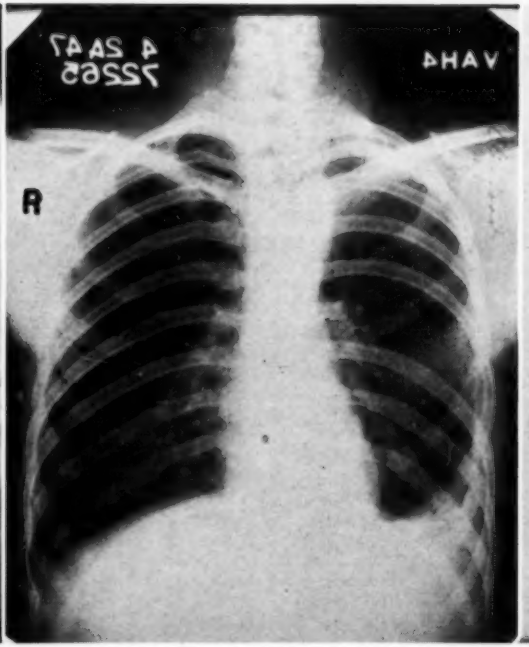


FIGURE 5

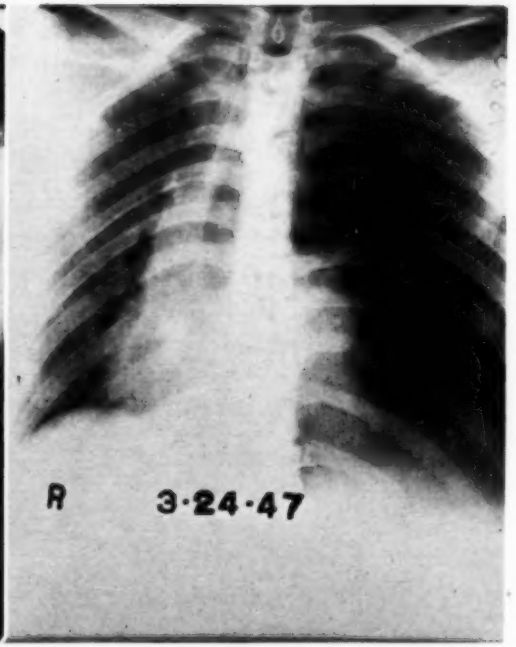


FIGURE 6

tioned before. The pneumothorax apparently occurred initially and was responsible for the sudden onset of symptoms. There evidently was but little, if any, bleeding into the pleural cavity for several hours. Upon admission to the hospital some 24 hours after onset of symptoms, there was blood in the pleural cavity and this accumulated rapidly during the next few hours. That this condition can constitute a medical emergency, and that conditions can change rapidly are borne out. Indications for prompt institution of therapeutic measures are well illustrated.

Case 2: A 31-year-old white male was hospitalized February 25, 1947. He had served in the peace time army in 1939-1940 and had been discharged with a diagnosis of psychoneurosis, neurasthenia. Between 1940 and 1946 he had complained of left chest pain and a complete study for chest disease was said to have been negative in January, 1946.

On February 15, 1947, ten days prior to admission, while driving a car over a bumpy backwoods road he complained of severe pain in the left chest. He continued to drive, but subsequently collapsed and was carried to his home. After failure of the usual home remedies to relieve his "indigestion,' a physician was called who told him that his heart was pushed to the right and that his left chest was full of fluid. He remained in bed without specific treatment during which time he complained of dyspnea, weakness, and a feeling which he described as "fluid flopping about" in the left chest. When he failed to improve, his doctor advised him to enter a hospital.

On admission he was critically ill with marked anemia. The red blood count was 1,600,000, the hemoglobin 30 per cent. There was a massive effusion in the left chest, with displacement of the mediastinum, the heart lying in the right midclavicular line (Fig. 3). Fever ranged from 102 to 105 degrees Fahrenheit the first few days, later dropping to around 100 degrees. Oxygen, penicillin and sedatives were given. During the first two weeks eleven thoracenteses were done with removal of 300 to 1,000 cc. of bloody, foul-smelling fluid, the total amount removed exceeding 5,000 cc. Six transfusions of 500 cc. of blood were given. Culture of the fluid was negative, as was the guinea pig inoculation for tubercle bacilli.

On March 13, 1947 he was transferred to another hospital where he was seen by one of us. On admission he complained only of left chest pain. He was pale, thin, and appeared chronically ill. The left chest was hyperresonant above the fourth rib posteriorly and dull below. Breath sounds were absent throughout the left side and expansion of the left chest was markedly diminished. Blood studies showed the red blood count 4,950,000, hemoglobin 83 per cent, white blood count 12,400 with normal differential count. Serological examination was negative as were sputum and chest fluid studies for acid-fast bacillus and tuberculin tests with purified protein derivative. Chest x-ray film (Fig. 4) showed complete collapse of the left lung, density over the entire left chest, with multiple levels of fluid and air. There was fever to 100 degrees Fahrenheit and some toxic manifestations with mental abnormalities of euphoria alternating with delusions of persecution which presented some difficulty of evaluation in view of a history of a previous suicidal attempt and other psychiatric abnormalities.

On March 25, 1947 a decortication of the left lung was performed by Drs. P. D. Elrod and J. D. Murphy through a parascapular incision with removal of a portion of the seventh rib. The pleural space was found to be filled with a fibrinous jelly-like mass with loculated pockets of wine-

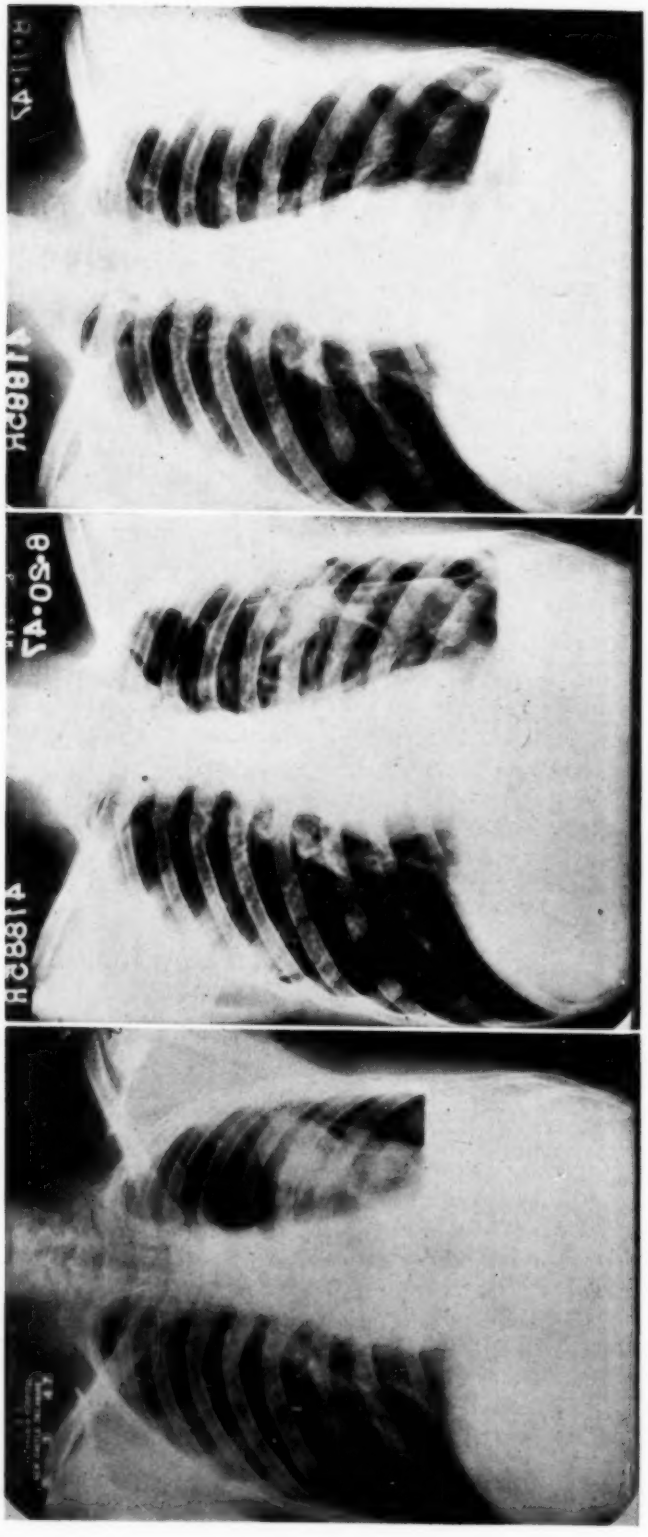


FIGURE 9

FIGURE 8

FIGURE 7

colored fluid. This was removed leaving a fibroblastic membrane covering the entire pleural surface. The lung was plastered against the mediastinum and pericardium. With blunt and sharp dissection this was separated from the visceral pleura and the diaphragm. The lung field was freed and its lobes separated. With slight positive pressure the lung was reexpanded and successfully filled the entire thoracic cavity. The chest cavity was closed and a catheter placed in the pleural cavity and connected to underwater drainage. This was removed one week later.

Pathologically the specimen removed consisted of two layers, one of fibrin and one of granulation tissue invaded by young capillaries.

Postoperatively there was rapid reexpansion of the lung and clearing of the pleural densities. Segmental breathing exercises were started one week postoperatively. The patient was free of symptoms and up and around the ward on the tenth postoperative day. A chest x-ray film on April 24, 1947 (Fig. 5) revealed blunting of the left costophrenic angle and some thickening of the pleura at the apex of the lung. The following day, one month postoperatively, he was discharged to his home.

Comment: This case appears to be the first reported instance of decortication for spontaneous hemopneumothorax. A massive hemorrhage associated with infection with neglect during the first ten days resulted in a completely collapsed and functionless lung. Aspiration was not successful and as a result of decortication five weeks after the initial bleeding, an excellent result was obtained. Examination of the encapsulating membrane clearly demonstrated the futility of considering conservative treatment.

Case 3: A 19-year-old white male was hospitalized on March 24, 1947. His previous medical history had been negative except that in 1924 he was advised to discontinue saxophone playing because a routine x-ray film showed a "scab on the lung." Apparently no other significance was attached to this finding at that time. He later served for 17 months in the navy and spent 14 months in the South Pacific area without illness.

March 17, 1947 he had a slight hemoptysis described as one spot of blood not more than one centimeter in diameter. On March 23 he awoke in the morning with pain in the epigastrium aggravated by coughing and deep breathing, with associated dyspnea. Nausea and vomiting were induced by self-administered ingestion of strong salt water.

When he was admitted on the next day to a hospital, x-ray film (Fig. 6) revealed a tension hydropneumothorax with marked mediastinal shift, the right cardiac border being in the right anterior axillary line by physical examination. Aspiration yielded bloody fluid. This was repeated three times at twelve-hourly intervals with symptomatic improvement; however, the tension pneumothorax with marked mediastinal shift persisted through April 3, 1947. Thoracenteses with the removal of 100 to 300 cc. of bloody fluid were repeated on April 4, 6, 8, and 21, but no attempt was made to remove all the blood, and a fluid level was allowed to remain above the level of the fifth posterior rib. Temperature was 104.4 degrees Fahrenheit on April 4, 1947 and did not return near normal until April 26, 1947. He had received penicillin and sulfadiazine therapy. The pleural fluid was sterile on three cultures. On April 30, the red blood count was 3,620,000, hemoglobin 77 per cent and white blood count 8,300 with 65 per cent neutrophils and 35 per cent lymphocytes.

May 1, 1947, 500 cc. of bloody fluid was removed, May 5, 150 cc. was aspirated and on each occasion 100,000 units of penicillin were instilled

and the pressure balanced. Further bleeding did not occur and the pneumothorax space remained dry. The fluid obtained was sterile. Chest x-ray film at this time (Fig. 7) revealed an extensive adhesion binding the lung to the chest wall in the upper mid-zone laterally. Because of slow reexpansion of the lung, bronchoscopy was performed on June 4, 1947. No endobronchial disease was demonstrated but the lumen of the left bronchus was reduced in size, without secretion. Reexpansion of the lung remained slow; therefore he was referred to another hospital for consideration of decortication on June 20, 1947, at which time he was seen by one of us.

There was found to be a sixty per cent collapse of the left lung with multiple adhesions extending to the chest wall and demonstrable thickening of the pleura (Fig. 8). Blood studies showed red blood count 4,990,000, hemoglobin 101 per cent, white blood count and differential count normal. The general condition was very good with a record of weight gain from 112 to 123 pounds during the previous six weeks. Decortication was considered but was not done because three months had lapsed since the onset, and organization and infiltration of the lung by the membrane was anticipated. In addition, slow but definite reexpansion had occurred between May 12 and June 20. Increased physical activity was encouraged and he was taught special unilateral breathing exercises under the supervision of the physiotherapist.

By August 12, 1947 virtually complete reexpansion had been obtained (Fig. 9) and a well marked friction rub was present in the lower axilla. Diminished expansion of the left chest and reduction of the vital capacity to 85 per cent of the calculated normal revealed gross evidence of impaired function of the left lung nearly five months after the onset of the hemopneumothorax. He was discharged to his home on August 13, 1947.

Comment: This is a case of a severe spontaneous hemopneumothorax with demonstrable adhesions put under tension by the collapse of the lung. This was presumably adequate to explain the bleeding. Early treatment was too conservative, as tension pneumothorax with mediastinal shift was allowed to persist for twelve days and aspirations were inadequate during the early treatment period so that a constricting pleuritis hampered reexpansion of the lung, with residual impairment of the respiratory capacity five months after the onset of the illness.

SUMMARY

Idiopathic spontaneous hemopneumothorax is presented as a medical emergency with serious potentialities, which is somewhat more common than the infrequency of reported cases would seem to indicate. The principles of treatment have been presented, both during the early period when life is endangered from the combination of massive hemorrhage and tension pneumothorax, and during the late stage when reexpansion of the lung is the primary problem. The importance of active treatment with aspirations, transfusions, oxygen and sedation, with judicious use of thoracic surgery is stressed. Three cases illustrating important applications of these treatment principles are described in detail.

RESUMEN

Se presenta el hemoneumotórax espontáneo idiopático como una emergencia médica que acarrea potencialidades graves y que es algo más común de lo que parecería indicarlo la rareza de los casos sobre los que se ha informado. Se han presentado los principios terapéuticos, tanto durante el período temprano cuando la combinación de hemorragia masiva y neumotórax hipertensivo amenazan la vida, como durante el período tardío cuando la reexpansión del pulmón es el problema primordial. Se recalca la importancia del tratamiento activo con punciones evacuadoras, transfusiones, oxígeno y sedantes y el empleo sensato de la cirugía torácica. Se describen en detalle tres casos que ejemplifican las importantes aplicaciones de estos principios terapéuticos.

REFERENCES

1 Hartzell, H. C.: "Spontaneous Hemopneumothorax: Report of Three Cases and Review of Literature," *Ann. Int. Med.*, 17:496, 1942.
2 Helwig, F. C. and Schmidt, E. C. H.: "Fatal Spontaneous Hemopneumothorax: Review of the Literature and Report of a Case," *Ann. Int. Med.*, 26:608, 1947.
3 Jennings, A. F.: "Spontaneous Hemopneumothorax," *Tr. Am. Clin. & Climatol. A. (1941)*, 57:107, 1942.
4 Tannenbaum, M.: "Spontaneous Hemopneumothorax, with Report of Case," *Dis. of Chest*, 8:178, 1942.
5 Snively, D., Shuman, H. W. and Snively, W. D.: "Spontaneous Hemopneumothorax; Case," *Ann. Int. Med.*, 16:349, 1942.
6 Franklin, J.: "Spontaneous Hemopneumothorax; Case Occurring in Soldier," *Ann. Int. Med.*, 23:437, 1945.
7 Lea, R. G.: "Spontaneous Hemopneumothorax," *Canad. M. A. J.*, 46: 371, 1942.
8 Payn, S. B. and Lief, V. F.: "Spontaneous Hemopneumothorax, Case," *Bull. U. S. Army Med. Dept.*, 84:94, 1945.
9 Waring, J. J.: "Spontaneous Hemopneumothorax," *Clinics*, 4:940, 1945.
10 Raimondi, A. A. and Boffi, L. L.: "Hemoneumotórax espontáneo," *Arch. argent. de tisiol.*, 19:331, 1943.
11 Leston, J. M. and Lamberti, C. E.: "Hemoneumotórax espontáneo," *Día méd.*, 15:1416, 1943.
12 Hopkins, H. O.: "Spontaneous Hemopneumothorax," *Am. J. Med. Sci.*, 193:763, 1937.
13 Personal communication from Dr. Hollis E. Johnson, Nashville, Tenn.
14 Personal communication from Dr. Sol Katz, Washington, D. C. (Cases in process of publication).

IX Congreso Panamericano del Niños

Caracas, Venezuela

First Section — Subject 3

PROPHYLAXIS OF INFANTILE TUBERCULOSIS

1) It was established that infantile tuberculosis must be maintained within the orbit of recognized fight against tuberculosis, such as the early discovery of the infectious cases and their segregation.

To achieve the first a recommendation made a year ago by the XII Conferencia Sanitaria Panamericana was adopted as follows:

It is recommended: A systematic and periodic examination of masses of people apparently healthy, by method fluorophotographic introduced by De Abreu, and when the resources do not permit the general examination, preference should be given to those groups considered, under an epidemiological study, as more affected. When this method is followed, also with the purpose of an epidemiological investigation, it must be complemented with tuberculin testing.

The intensification of this procedure must not be done in detriment to the work of the Dispensary, which is the present base for the fight against tuberculosis.

To enlarge the field of case finding activities, there must be promoted methods of teaching that will capacitate the general practitioner for the achievement of this purpose.

To carry the segregation correctly, it is believed, that it is indispensable to allot for the fight against tuberculosis the necessary number of hospital beds according to the possibilities of each country, omitting other institutional types as preventoriums.

2) It is believed that resistance to tuberculosis can be increased by indirect measures of non-specific nature or by direct ones of specific character.

The first are all that tends to raise the standard of living, have the first consideration, emphasizing, when dealing with children on matters of education.

The second, are represented until the present time by the BCG vaccination, the use of which is advised as part of the Sanitary Administration as an effective and already recognized prophylactic measure without interference with others.

It is recommended the formation of an International Commission of Bacteriologists, physicians and statisticians to study means for standardization of production, make use and estimation of its value.

3) It is recommended that greater attention be given than the one at present in some countries of the American Continent to the control and eradication of bovine tuberculosis.

Fifteenth Annual Meeting

AMERICAN COLLEGE OF CHEST PHYSICIANS

Arrangements have been completed for the Fifteenth Annual Meeting of the American College of Chest Physicians to be held at the Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1949. Advance reservations for hotel accommodations indicate that the meeting will exceed all past attendance records. Every effort is being made by the Committee on Housing to accommodate members of the College who wish to attend the College meeting, as well as the Annual Meeting of the American Medical Association.

The Committee on Scientific Program has arranged excellent scientific sessions on all phases of diseases of the chest. Some of the features this year will be: Informal round table luncheon meetings; critical reviews of current developments in the specialty of diseases of the chest; a motion picture session; and an x-ray conference. There will also be luncheon meetings devoted to medical education, tuberculosis hospital standards and international affairs.

Oral and written examinations for Fellowship in the College and the following administrative sessions will be held at the Ambassador Hotel:

THURSDAY, JUNE 2

8:00 a. m. Board of Examiners.

9:00 a. m. Oral Examinations.

2:00 p. m. Written Examinations.
Candidates are requested to report to the Board of Examiners at 8:30 a. m.

8:00 a. m. Executive Council and Committee on Certification.

10:00 a. m. Annual Meeting, Board of Governors.

12:00 noon Luncheon Meeting.
Annual Conference of College Chapter Officials.

1:30 p. m. Committee on College By-Laws.

2:00 p. m. Annual Meeting, Board of Regents.

2:00 p. m. Council on Public Health,
Committee on Chest Diseases in Penal and Mental Institutions.
Committee on Occupational Diseases of the Chest.

2:00 p. m. Council on the Management of Diseases of the Chest,
Committee on Surgical Treatment of Diseases of the Chest.
Committee on Non-Surgical Collapse Therapy.
Committee on Chemotherapy and Antibiotics.

5:00 p. m. Council on Public Relations.

7:00 p. m. Committee on Nominations.

7:00 p. m. Council of Tuberculosis Committees.

7:00 p. m. Council on Undergraduate Medical Education.

8:00 p. m. Council on Postgraduate Medical Education.

8:00 p. m. Council on International Affairs.

SECOND ANNUAL POSTGRADUATE COURSE IN DISEASES OF THE CHEST, AMERICAN COLLEGE OF CHEST PHYSICIANS
February 28 - March 4, 1949, Warwick Hotel, Philadelphia, Pennsylvania

Some of the physicians and instructors who participated in the Postgraduate Course in Diseases of the Chest held in Philadelphia.

FRIDAY, JUNE 3

8:00 a. m. Editorial Board.
4:00 p. m. Council of Tuberculosis Hospitals,
Committee on Sanatorium Standards.
Committee on Rehabilitation.
5:00 p. m. Council on Research.

SATURDAY, JUNE 4

9:00 a. m. Administrative Session (Open to all members of the College),
Report of the Historian.
Report of the Treasurer.
Report of the Executive Secretary.
Report of the Committee on Certification.
Election of Officers.
Reports of Councils and Committees.

SUNDAY, JUNE 5

5:00 p. m. Meeting, Board of Regents.

The scientific sessions will begin on Friday morning, June 3rd at 9:00 a. m., and continue through Saturday, June 4th and Sunday, June 5th.

At 6:00 p. m. on Saturday, June 4th, the College Convocation will be held. The Convocation will be followed by the Social Hour and Annual Presidents' Banquet.

A convenient coupon for hotel reservations is published on page xiv of the advertising section in this issue.

Second Annual Postgraduate Course in Diseases of the Chest Presented in Philadelphia

The Second Annual Postgraduate Course in Diseases of the Chest was presented at the Warwick Hotel, Philadelphia, under the sponsorship of the American College of Chest Physicians and the Laennec Society of Philadelphia, February 28-March 4, 1949. There were 44 physicians registered in the course representing 17 states, the District of Columbia, Canada, Argentina and Brazil.

College Chapter News

ARGENTINE CHAPTER

On December 11, 1948, the Argentine Chapter of the College held its annual meeting in Cordoba. An excellent scientific program on the use of streptomycin in the treatment of pulmonary tuberculosis was presented. The following members of the Chapter presented papers: Dr. Tomás de Villafañe Lastra, Dr. Rodolfo Cuchiani Acevado, Dr. Isaac A. Hassan, and Dr. Rómulo Muzzio. After the scientific program the election of officers for 1949 took place. The new officers for the Argentina Chapter are:

Justo Lopez Bonilla, M.D., Rosario, President
Oscar A. Vaccarezza, M.D., Buenos Aires, Vice-President
Abraham F. Schottlender, M.D., Rosario, Secretary-Treasurer.

ARIZONA CHAPTER

The Arizona Chapter of the College will hold its annual meeting on May 10 in conjunction with the annual meeting of the Arizona State Medical Association, May 8-11, at Tucson. The following program will be presented:

"Pulmonary Resection in Tuberculosis—Indications and Results,"
Reginald Smart, M.D., F.C.C.P., Los Angeles, California.

"Mediastinal Tumors,"
Thomas B. Wiper, M.D., F.C.C.P., San Francisco, California.

CALIFORNIA CHAPTER

The annual meeting of the California Chapter of the College will be held at the Biltmore Hotel, Los Angeles, on Saturday, May 7, commencing at 2:00 p. m. The following program will be presented:

"Pneumonia in Southern California,"
Roger Egeberg, M.D., Los Angeles.

"Resistance Studies to Antibiotics in Tuberculosis,"
Edward Dunner, M.D., F.C.C.P., Livermore.

"Conservation on Chemotherapy in Tuberculosis,"
Emil Bogen, M.D., F.C.C.P., Olive View.

"Peripheral Vascular Disease in Chronically Ill Patients,"
Elise Rose, M.D., San Francisco.

MICHIGAN CHAPTER

At the meeting of the Michigan Chapter of the College held on February 11th at the Detroit Tuberculosis Sanatorium the following officers were elected for the ensuing year:

William P. Chester, M.D., Detroit, President
Cletus J. Golinvaux, M.D., Monroe, Vice-President
Constantine P. Mehas, M.D., Pontiac, Secretary-Treasurer.

Dr. Chester presented a talk on pneumoconiosis and several members recited their experiences with this disease.

MISSOURI CHAPTER

At the annual meeting of the Missouri Chapter of the College held in Kansas City on March 26th th following officers were elected:

Alfred Goldman, M.D., St. Louis, President
Charles A. Brasher, M.D., Mt. Vernon, Vice-President
A. J. Steiner, M.D., St. Louis, Secretary-Treasurer.

PORTUGUESE CHAPTER ORGANIZED

The organizational meeting of the Portuguese Chapter was held in Lisbon on March 28th. Professor Lopo de Carvalho, Governor of the College for Portugal, presided at the meeting.

NEW YORK STATE CHAPTER

The New York State Chapter of the College will hold its annual meeting in Buffalo in conjunction with the annual meeting of the New York State Medical Society, May 5-6, 1949. The following program will be presented in the Section on Chest Diseases of the New York State Medical Society:

"Mediastinal Emphysema with Spontaneous Pneumothorax,"
Donald R. McKay, M.D., F.C.C.P., Buffalo.
Discussant: David Ulmar, M.D., F.C.C.P., New York City.

"Present Views on Streptomycin Therapy in Pulmonary Tuberculosis,"
William H. Stearns, M.D., New York City.
Discussant: Nicholas D. D'Esopo, M.D., Sunmount.

"Experiences with Intracavity Drainage (Monaldi) in Pulmonary Tuberculosis,"
Warriner Woodruff, M.D., Saranac Lake.
Discussant: Allan Strahahan, M.D., Albany.

"Exact Diagnosis of Pulmonary Tuberculosis,"
Herman E. Hilleboe, M.D., F.C.C.P., Albany.
Discussant: Nelson Strohm, M.D., F.C.C.P., Buffalo.

"Diaphragmatic Hernia,"
Herbert W. Meyer, M.D., New York City.
Discussant: John A. Stewart, M.D., Buffalo.

"Bronchostenosis in Limited Pulmonary Tuberculosis,"
Edward N. Packard, M.D., Trudeau.
Discussant: George W. Wright, M.D., F.C.C.P., Trudeau.

"Mediastinal Packing in the Treatment of Esophageal Varices,"
John Garlock, M.D., New York City.
Discussant: Max Som, M.D., New York City.

"Decortication of the Lung in Non-Traumatic Lesions,"
Herbert C. Maier, M.D., and W. Fischer, M.D., New York City.
Discussant: Lew A. Hochberg, M.D., F.C.C.P., Brooklyn.

Dr. Foster Murray, Brooklyn, and Dr. Samuel A. Thompson, New York City, are Chairman and Secretary, respectively, of the Section on Chest Diseases in the New York State Medical Society.

College News Notes

Dr. Angel Gines, Governor of the College for Paraguay, has been appointed Professor of Clinical Medicine in the Faculty of Medical Sciences, Asuncion.

Dr. Edward P. Eglee, New York City, has been elected chairman of the executive committee of the New York Tuberculosis and Health Association.

Professor Tevfik Saglam has been appointed Governor of the College for Turkey. Professor Saglam is also a member of the newly created Council on African and Near East Affairs of the College.

At the annual meeting of the National Conference on Medical Service, held in Chicago, February 6, Dr. Walter E. Vest, Huntington, West Virginia, was elected a member of the executive committee. Dr. John S. Bouslog, Denver, Colorado, was named president of the Conference.

Obituary

EUSTACE THOMAS GOFF
1886-1948

Dr. Eustace Thomas Goff, 62, of Parkersburg, West Virginia, died at his home in that city November 22, 1948, following a heart attack. Death was unexpected.

Dr. Goff, whose specialty was diseases of the chest, was born at Hazel Green, West Virginia. He received his academic training at West Virginia University and graduated from the Medical College of Virginia in 1913. After engaging in practice at Smithville and Clarksburg, he moved to Parkersburg in 1922, where he remained in active practice until his death.

Dr. Goff was a Fellow of the American College of Chest Physicians, a member of the Academy of Medicine of Parkersburg, the West Virginia State Medical Association, and the American Medical Association.

G. R. Maxwell, M.D., Governor for West Virginia.

Book Review

INFANTILE TUBERCULOSIS, by Pierre Lowys. Preface by Professor Debre. Published by Flammarion, Paris, 1948.

The book presents a complete treatise on infantile tuberculosis, as useful to the practising physician to whom it brings everything he should know, as to the pediatrician or tuberculosis specialist, who will find in it the solution of all the questions bearing on the subject.

Having explained his modern conception of the evolution of tuberculous disease, and shown how the infant becomes tuberculous, Lowys discusses the clinical aspects, the development, the prognosis, the allergic manifestations, the tuberculin reactions and their variations, the laboratory data and their significance, illustrating the chapter on radiology by a number of plates. The differential diagnosis is presented from a specially critical and practical viewpoint.

The second half of the book is devoted to treatment (medical, collapse therapy, surgical, prophylactic). No detail is left uncovered. Based upon the observation of 2,000 infants, of 20,000 plates of the chest, at the sanatorium of Rocdes—Fiz (Passy, Hte Savoie), arising from the particularly careful and benevolent experience of a pioneer in infantile tuberculosis as is Lowys, this book is an epoch making document.

Paul Veran, M.D., Nantes, France.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS

The Sixty-First Annual Meeting of the American Association of Railway Surgeons will be held at the Drake Hotel, Chicago, Illinois, on Thursday, June 30, Friday, July 1, and Saturday morning, July 2, 1949.